A.M.A. Journal OF
DISEASES OF CHILDREN

Parathyroid Adenoma in a Child — *Mary Harmon*

Muscular Dystrophy

I. History, Clinical Status, Muscle Strength, and Biopsy Findings
G. H. Fetterman, M. J. Wretney, J. S. Donaldson, and T. S. Danowski

II. Radiologic Findings in Relation to Severity of Disease
B. Girdany and T. S. Danowski

III. Serum and Blood Solutes and Other Laboratory Indices
T. S. Danowski, P. M. Wirth, M. H. Leinberger, L. A. Randall, and J. H. Peters

IV. Endocrine Studies
T. S. Danowski, R. M. Bastiani, F. D. McWilliams, F. M. Mateer, and L. Greenman

Adrenal Pheochromocytoma Simulating Diabetes Insipidus — *Fethi Tevetoğlu and Chi-Hao Lee*

Typhoid with Meningitis (Salmonella Typhosa)
Sam M. Powell

Complete Contents on First Inside Page

APRIL 1956

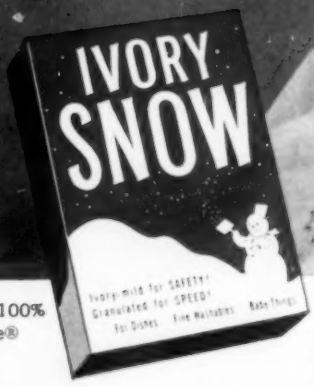
VOLUME 91 NUMBER 4

From: Girdany and Danowski, p. 339

AMERICAN MEDICAL ASSOCIATION Publication

IVORY SNOW

Safe and mild as a soap can be for diapers and baby things



99 44/100% Pure®

When diapers and baby clothes are washed in Ivory-safe Ivory Snow, they come out soft, smooth, free from irritating deposits that might chafe a baby's skin. And—because Ivory Snow is in the efficient granulated form preferred for washing-machine use—it's a practical soap for busy mothers with lots of baby wash to do.

A Procter & Gamble Product

TABLE OF CONTENTS

VOLUME 91 APRIL 1956 NUMBER 4

ORIGINAL ARTICLES

Parathyroid Adenoma in a Child PAGE

Mary Harmon, M.D., Cleveland 313

Muscular Dystrophy

I. History, Clinical Status, Muscle Strength, and Biopsy Findings

G. H. Fetterman, M.D.; M. J. Wratney, B.S., M.Ed.; J. S. Donaldson, M.D., and T. S. Danowski, M.D., Pittsburgh 326

II. Radiologic Findings in Relation to Severity of Disease

B. Girdany, M.D., and T. S. Danowski, M.D., Pittsburgh 339

III. Serum and Blood Solutes and Other Laboratory Indices

T. S. Danowski, M.D.; P. M. Wirth; M. H. Leinberger, B.S.; L. A. Randall, and J. H. Peters, M.D., Pittsburgh 346

IV. Endocrine Studies

T. S. Danowski, M.D.; R. M. Bastiani; F. D. McWilliams; F. M. Mateer, M.D., and L. Greenman, M.D., Pittsburgh 356

Adrenal Pheochromocytoma Simulating Diabetes Insipidus

Fethi Tevetoğlu, M.D., and Chi-Hao Lee, M.D., Corpus Christi, Texas 365

CASE REPORTS

Typhoid with Meningitis (Salmonella Typhosa)

Sam M. Powell, M.D., Corpus Christi, Texas 380

OBITUARIES

Isaac Arthur Abt, M.D. 385

REGULAR DEPARTMENTS

Abstracts from Current Literature 387

News and Comment 384, 408

Books:

Books Received 410

Book Reviews 412

A. M. A.
Journal of Diseases of Children

VOLUME 91 APRIL 1956 NUMBER 4

COPYRIGHT, 1956, BY THE AMERICAN MEDICAL ASSOCIATION

EDITORIAL BOARD

ROBERT B. LAWSON, Chief Editor
1000 N. W. 17th St., Miami 36, Fla.

ROBERT A. ALDRICH, Portland, Ore.
RICHARD L. DAY, Brooklyn
ROGER L. J. KENNEDY, Rochester, Minn.
FRANCIS SCOTT SMYTH, San Francisco
A. A. WEECH, Cincinnati
WARREN E. WHEELER, Columbus, Ohio
JAMES L. WILSON, Ann Arbor, Mich.
WOLF W. ZUELZER, Detroit

AUSTIN SMITH, Editor, A. M. A. Scientific Publications
GILBERT S. COOPER, Managing Editor, Specialty Journals

AMERICAN MEDICAL ASSOCIATION SCIENTIFIC PUBLICATIONS

A. M. A. Specialty Journals

Monthly

A. M. A. Archives of Internal Medicine. Paul S. Rhoads, M.D., Chief Editor, American Medical Association, 535 N. Dearborn St., Chicago 10. Price, $10.00; Canada, $10.50; Foreign, $11.50; individual copy, $1.00.*

A. M. A. Archives of Dermatology. Herbert Rattner, M.D., Chief Editor, 104 S. Michigan Ave., Chicago. Price, $12.00; Canada, $12.50; Foreign, $13.50; individual copy, $1.25.†

A. M. A. Archives of Ophthalmology. Francis Heed Adler, M.D., Chief Editor, 313 S. 17th St., Philadelphia 5. Price, $12.00; Canada, $12.50; Foreign, $13.50; individual copy, $1.25.†

A. M. A. Archives of Surgery. Waltman Walters, M.D., Chief Editor, American Medical Association, 535 N. Dearborn St., Chicago 10. Price, $14.00; Canada, $14.50; Foreign, $15.50; individual copy, $1.25.‡

A. M. A. Journal of Diseases of Children. Robert B. Lawson, M.D., Chief Editor, 1000 N. W. 17th St., Miami 36, Fla. Price, $12.00; Canada, $12.50; Foreign, $13.50; individual copy, $1.25.†

A. M. A. Archives of Pathology. Paul R. Cannon, M.D., Chief Editor, Department of Pathology, University of Chicago, The School of Medicine, 950 E. 59th St., Chicago 37. Price, $10.00; Canada, $10.50; Foreign, $11.50; individual copy, $1.00.*

A. M. A. Archives of Neurology and Psychiatry. Harold G. Wolff, M.D., Chief Editor, Neurology, 525 E. 68th St., New York 21; Roy R. Grinker Sr., M.D., Chief Editor, Psychiatry, Institute for Psychosomatic and Psychiatric Research, 29th St. and Ellis Ave., Chicago 16. Price, $14.00; Canada, $14.50; Foreign, $15.50; individual copy, $1.50.‡

A. M. A. Archives of Otolaryngology. George M. Coates, M.D., Chief Editor, 1721 Pine St., Philadelphia 3. Price, $14.00; Canada, $14.50; Foreign, $15.50; individual copy, $1.50.‡

A. M. A. Archives of Industrial Health. Prof. Philip Drinker, Chief Editor, Dept. of Industrial Hygiene, Harvard University School of Public Health, 55 Shattuck St., Boston 15. Price, $10.00; Canada, $10.50; Foreign, $11.50; individual copy, $1.00.*

* Price to students, interns, and residents: $6.00 in U. S. & possessions.

† Price to students, interns, and residents: $7.00 in U. S. & possessions.

‡ Price to students, interns, and residents: $8.00 in U. S. & possessions.

The price for individual copies applies only to this and the previous calendar year; 5 cents additional is charged for each year preceding the last calendar year.

The Journal of the American Medical Association. Weekly. Annual Subscription Price: Domestic, $15.00. Canadian, $17.00. Foreign, $21.50. Price to students, interns, and residents: $9.00 in U. S. & possessions.

Quarterly Cumulative Index Medicus. Issued Twice a Year. Subscription Price, Calendar year, $25.00.

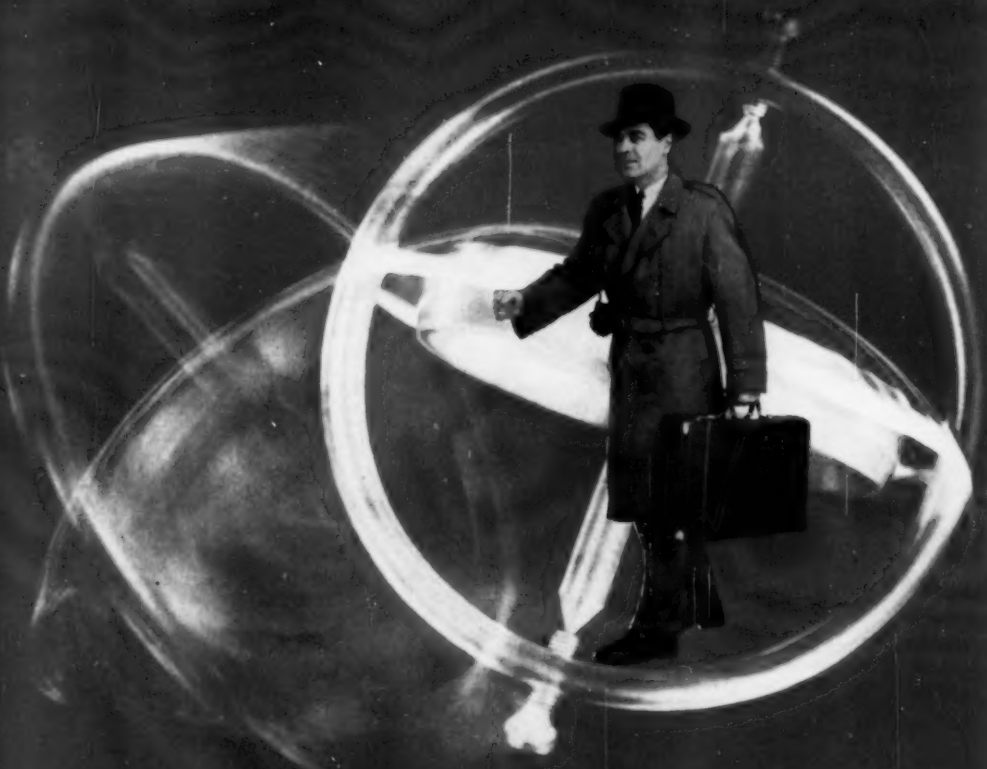
Checks, money orders, and drafts should be made payable to the American Medical Association, 535 North Dearborn Street, Chicago 10.

Published Monthly by

AMERICAN MEDICAL ASSOCIATION

535 NORTH DEARBORN STREET • CHICAGO 10, ILLINOIS

Entered as Second Class Matter Jan. 4, 1911, at the Postoffice at Chicago, Under the Act of March 3, 1879. Annual Subscription, $12.00



stabilized with

Bonamine

Long-acting motion-sickness remedy, often effective in a single daily dose; for trouble-free travel on land and sea and in the air.

BONAMINE TABLETS, *scored, tasteless, 25 mg.*

BONAMINE CHEWING TABLETS, *pleasantly mint flavored, 25 mg.*

*Trademark

Pfizer

PFIZER LABORATORIES, *Division, Chas. Pfizer & Co., Inc.*, Brooklyn 6, N. Y.

Instructions to Contributors

Communications regarding editorial management, subscriptions, reprints, etc., should be addressed to Specialty Journals, American Medical Association, 535 North Dearborn Street, Chicago 10.

Articles, book reviews, and other materials for publication should be addressed to the Chief Editor of the Specialty Journal concerned. Articles are accepted for publication on condition that they are contributed solely to that journal.

An original typescript of an article should be provided; it must be double or triple spaced on one side of a standard size page, with at least a 1-inch margin at each edge. A carbon copy should be retained by the author. An article in English by a foreign author should be accompanied by a draft in the author's mother tongue. Improvised abbreviations should be avoided.

The main title of an article may not contain more than seventy characters and spaces; a subtitle may be of any length. The subtitle should be sufficiently detached from the main title that a punctuation mark as strong as a colon can be used in the Table of Contents to separate it from the main title; it must not begin with "with."

The author's name should be accompanied by the highest academic or medical degree which he holds. If academic connections are given for one author of an article, such connections must be given for all other authors of the article who have such connections.

A Case Report must be preceded by an introductory paragraph containing at least thirty words before the details of the case are given. To avert the possibility of legal action, patients' initials and hospital case numbers should not be published.

Material quoted from another publication must be quoted exactly if the original is in English—spelling, capitalization, punctuation, etc., unchanged. Material taken largely from another publication must be credited to the original author, whether quoted exactly or merely abstracted.

Each article should be accompanied by a summary in the present tense, presenting the main points of the article, but in somewhat more generalized terms than in the article itself.

If it is necessary to publish a recognizable photograph of a person, the photograph must be accompanied by written permission of the subject himself if an adult, or of the parents or guardian if a child, to publish his photograph. An illustration which has been published in another publication must be accompanied by written permission from the author and the original publisher to reproduce it in an A. M. A. Specialty Journal.

The maximum illustration allowance is ten illustrations within a total of 100 sq. inches or $100, whichever is of greater advantage to the author. When no restrictions are placed by the author upon cropping, reducing, and grouping, the publisher is often able to use twenty or more illustrations in one article with the $100 allowance. See an issue of this journal for examples. Oversized originals should be photographed and a print submitted. Large photomicrograph prints will be reduced in scale unless portions to be cropped are indicated by the author.

Any cut-off marks should be made on the margins (or mountings) rather than on the illustration itself. Charts and drawings should be in black ink on hard, white paper. Lettering must be large enough to permit necessary reduction. Glossy prints of x-rays are requested. Paper clips should not be used on prints, since their mark shows in reproduction, as does writing on the back of prints with hard lead pencil or stiff pen. Labels should be prepared and pasted to the back of each illustration showing its number, the author's name, an abbreviated title of the article, and top plainly indicated. Charts and illustrations must have descriptive legends, grouped on a separate sheet. Tables must have captions. ILLUSTRATIONS SHOULD BE UNMOUNTED.

References to the literature should be numbered in the order in which they are referred to in the text or listed in alphabetical order without numbers. A chronological arrangement, with all entries for a given year alphabetized according to the surname of the first author, may be used if preferred. References should be typed on a special page at end of manuscript. They should conform to the style of the Quarterly Cumulative Index Medicus, and must include, in the order given, name of author, title of article (with subtitle), name of periodical, with volume, page, month—day of month if weekly or biweekly—and year. Names of periodicals should be given in full or abbreviated exactly as in the Quarterly Cumulative Index Medicus. Reference to books must contain, in the order given, name of author, title of book, city of publication, name of publisher, and year of publication. Titles of foreign articles, if originally in a generally known Romance or Germanic tongue, must either all be in English translation or all be in the original language. Titles in other languages must be translated. The author must assume responsibility for the accuracy of foreign titles.

Matter appearing in the A. M. A. Specialty Journals is covered by copyright, but as a rule no objection will be made to its reproduction in a reputable medical journal if proper credit is given. However, the reproduction for commercial purposes of articles appearing in the A. M. A. Specialty Journals, or in any other publications issued by the Association, will not be permitted.

AMERICAN MEDICAL ASSOCIATION

535 North Dearborn Street **Chicago 10**

New urethral suppositories relieve pain and combat infection

***The child's activities continue—treatment is "...shorter and more comfortable than the conventional method..."*[1]**

- relieve pain and burning promptly
- kill most bacteria common to urethral infections
- easy for mother to insert at home
- irritation rare in over 340 cases (adults)[1]

PRESCRIBE: for bacterial (granular) urethritis, for topical anesthesia and prophylaxis of infection before and after instrumentation

FURACIN vaginal suppositories

To prevent urethrovaginal cross-infection, "Furacin suppositories are inserted in the urethra daily, if practical, and inserted in the vagina each night for a week."[2] Formula: Furacin, 0.2% in a water-miscible base.

References: 1. Youngblood, V. H.: J. Urol. 70:928, 1955. 2. Carroll, G.: Pediat. Clin. N. America, 1955, pp. 781-791.

FURACIN®
BRAND OF NITROFURAZONE
urethral
SUPPOSITORIES

Formula. 0.2% Furacin (brand of nitrofurazone), 2% diperodon•HCl in water-miscible base. Sealed in foil. Box of 12.

EATON LABORATORIES, Norwich, N.Y. **NITROFURANS** a new class of antimicrobials neither antibiotics nor sulfas

FOUR IMPORTANT TOOLS AT

YOUR COMMAND

. . . each effective against a specific seizure type

TRIDIONE®
(TRIMETHADIONE, ABBOTT)

an agent of choice in the* petit mal *triad

First successful synthetic anticonvulsant—now an agent of choice—for symptomatic control of *petit mal*, myoclonic and akinetic seizures.

PARADIONE®
(PARAMETHADIONE, ABBOTT)

homologue to Tridione

An alternative preparation which is often effective in cases refractory to Tridione therapy. Especially for treatment of the *petit mal* triad.

PHENURONE®
(PHENACEMIDE, ABBOTT)

often successful where other therapy fails

A potent anticonvulsant to be used with discretion for *psychomotor epilepsy, grand mal, petit mal* and mixed seizures. Has succeeded when other therapy has failed.

GEMONIL®
(METHARBITAL, ABBOTT)

a drug of low toxicity

The newest of Abbott's anticonvulsant drugs. For *grand mal, petit mal, myoclonic* and mixed seizures. Effective in disorders symptomatic of organic brain damage.

Send for literature to Abbott Laboratories, North Chicago, Illinois

Abbott

604140

Truly portable, all-purpose unit providing dependable respirator facilities . . . wherever, whenever needed . . . in transit, in the home, in the hospital.

Bulletin No. MA-1 gives details of Hospital and Portable models. We'll be glad to send it to you.

dependable mobility for the respirator patient

freedom for transport by train or plane, using their 24 volt current directly

freedom to enjoy the out-of-doors . . . to take it easy in the sun

elements of the unit

freedom to go places . . . to take trips . . . to "visit"

technicon-huxley • **chest-abdomen portable respirator**

Conitech, LTD.
Chauncey • New York

operates on { house current or 24 volt DC or its own battery

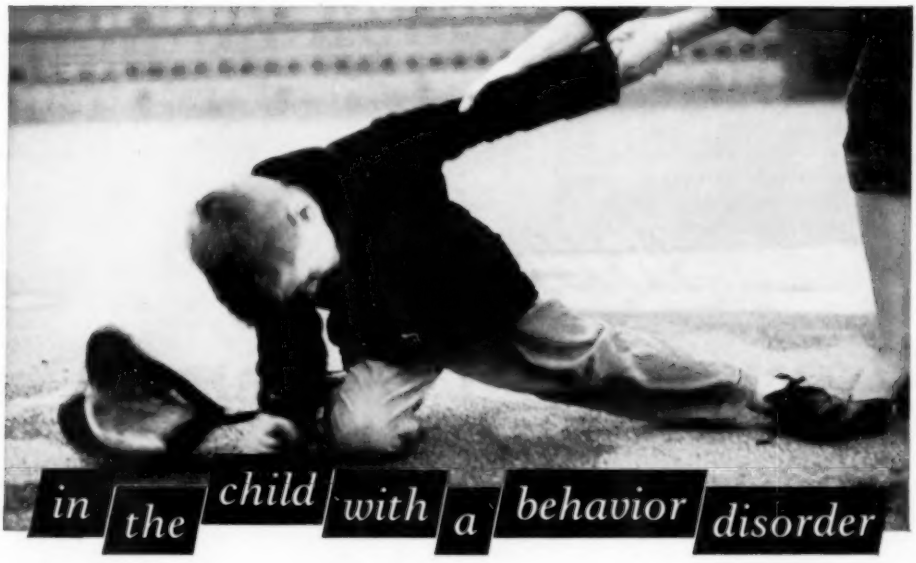
This symbol on the inner sole of a shoe identifies Selby Juniors... the only genuine Arch Preserver Shoes for children

• *If Selby Junior Arch Preservers are not available in your city, please write directly to us.*

The Selby Shoe Company
Portsmouth, Ohio

Selby
JUNIOR ARCH PRESERVER
Shoes

MORE THAN THREE QUARTERS OF A CENTURY OF FINE SHOEMAKING



THORAZINE*

reduces hyperactivity and aggressiveness

decreases anxiety and hostility

improves mood, behavior and sleeping habits

establishes accessibility to guidance or psychotherapy

increases amenability to supervision

FACTS TO BEAR IN MIND Even though the dramatic calming effect of 'Thorazine' on belligerent, overactive children may give the impression of a cure, simultaneous supportive counseling and guidance are necessary if lasting benefits are to be assured.

Adequate 'Thorazine' dosage for certain seriously disturbed youngsters will sometimes exceed 50-100 mg. t.i.d.

'Thorazine' should be administered discriminately and, before prescribing, the physician should be fully conversant with the available literature.

'Thorazine' is available in ampuls, tablets and syrup (as the hydrochloride), and in suppositories (as the base).

Smith, Kline & French Laboratories, Philadelphia

*T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.

little

How to win friends ...

The Aspirin that Tastes So Good.

The Flavor Remains Stable down to the last tablet.

15c Bottle of 24 tablets (2½ grs. each).

We will be pleased to send samples on request.

THE BAYER COMPANY DIVISION of Sterling Drug Inc. 1450 Broadway, New York 18, N. Y.

when you must combine...

...and the many other conditions coordinate with anxiety, tension and emotional upset

prescribe compatible

pleasant-tasting
highly compatible liquid
compounded with...
other agents
of your choice

The antihypertensive and tranquilizing effects of Serpasil can now be easily combined with other agents that you may wish to prescribe simultaneously. Serpasil Elixir is compatible with many other medications, such as Pyribenzamine® citrate (tripelennamine citrate CIBA) Elixir, dextro-amphetamine sulfate elixir, codeine phosphate, ephedrine sulfate, and sodium salicylate.

Each 4-ml. teaspoonful of light green, lemon-lime flavored Serpasil Elixir contains 0.2 mg. of Serpasil.

CIBA
Summit, N. J.

YOUR
GUIDE TO
CURRENT PUBLICATIONS

Quarterly Cumulative Index Medicus

WITH AUTHORS AND SUBJECTS . . .

Divided into sections, one devoted to books and the other to periodical literature, the QUARTERLY CUMULATIVE INDEX MEDICUS contains a list of current publications alphabetized as to authors and subjects. The exact bibliographic reference is given under the author with titles in the original language, while titles under subjects are all in English. The index also includes a listing of journals, addresses and publishers.

The QUARTERLY CUMULATIVE INDEX MEDICUS appears twice a year; volumes are cloth bound and cover periodicals for six months as indicated on the publication. These two volumes will be a convenient and inclusive reference for current medical literature. Invaluable for practitioners, specialists, teachers, editors, writers, investigators, students and libraries.

SUBSCRIPTION PRICE $25.00 PER YEAR
CANADIAN AND FOREIGN $27.00 PER YEAR

AMERICAN MEDICAL ASSOCIATION
535 NORTH DEARBORN STREET
CHICAGO 10, ILLINOIS

Enriched Bread... and Child Health in America

The enrichment of commercial white bread with thiamine, riboflavin, niacin, and iron is one of the important factors in the improvement of nutrition in America's school children.[1] Improved nutrition appears to have made a valuable contribution to the improvement of child health during recent years.[2]

Containing nonfat milk solids (usually 4 lbs. per 100 lbs. of flour) as well as officially defined amounts of B vitamins and iron, enriched bread provides high percentages of recommended daily dietary allowances for children.

The protein of enriched bread, an aggregate of flour, milk, and yeast proteins, is high in nutritive quality, effective for growth as well as tissue maintenance. On the basis of its percentage of calories provided, enriched bread supplies substantially more than its share of niacin, thiamine, and iron, and a goodly proportion of riboflavin and calcium. Because enriched bread presents carbohydrate and good quality protein simultaneously, the carbohydrate thereby "sparing" protein, it helps promote optimum protein anabolism.[3] For all these reasons, enriched bread constitutes a valuable asset to good nutritional health in children.

1. Bowes, A. deP.: Dietotherapy—Nutrition of Children During Their School Years, Am. J. Clin. Nutrition 3: 254 (May-June) 1955.
2. Kelly, H. T.: Impact of Modern Nutrition on Twentieth Century Morbidity, Pennsylvania M. J. 58: 481 (May) 1955.
3. Cantarow, A., and Trumper, M.: Clinical Biochemistry, ed. 5, Philadelphia, W. B. Saunders Company, 1955, pp. 139, 140.

Percentages of Recommended Daily Dietary Allowances* for Children Provided by Enriched Bread—6 and 8 slices

	Children Ages 4 to 6 years		Children Ages 7 to 9 years	
	6 slices	8 slices	6 slices	8 slices
Protein	23%	31%	20%	26%
Niacin	38	50	30	40
Riboflavin	18	23	14	19
Thiamine	41	55	33	44
Calcium	12	16	12	16
Iron	41	55	33	44
Calories	24	32	19	25

*National Research Council's recommended daily dietary allowances (1953):
Children, 4 to 6 years of age; weight, 40 lbs.; height, 43 inches.
Children, 7 to 9 years of age; weight, 59 lbs.; height, 51 inches.

AMERICAN BAKERS ASSOCIATION
20 NORTH WACKER DRIVE • CHICAGO 6, ILLINOIS

The nutritional statements made in this advertisement have been reviewed by the Council on Foods and Nutrition of the American Medical Association and found consistent with current authoritative medical opinion.

diaper-size diets?

The troubles of adult mankind may sometimes beset their young. And, while there may be some consolation in the fact that a baby on a diet cannot bore listeners with what he or she can or can't eat, *special diets* for the diaper set are by no means a small-size problem.

For many of those diaper-size diet problems, though, *Instant* Pet Nonfat Dry Milk has proved very helpful. Since it provides all the protein, calcium, and B-vitamins of milk in concentrated form, it can be an ideal base for special-formula requirements.

When diarrhea or digestive disturbances make formula adjustment necessary . . . when infant needs call for higher solids content (as in feeding of prematures) . . . when a low-fat formula is desirable . . . *Instant* Pet is most helpful in providing a satisfactory answer.

And, particularly important to the parents of special-diet babies, *Instant* Pet costs much, much less than special-formula preparations . . . less, in fact, than any other form of milk for infant feeding.

***Instant* PET NONFAT DRY MILK**
. . . for your special infant feeding cases

PET MILK COMPANY • ARCADE BUILDING • ST. LOUIS 1, MISSOURI

A.M.A. Journal OF DISEASES of CHILDREN

Parathyroid Adenoma in a Child

Report of a Case Presenting as Central Nervous System Disease and Complicated by Magnesium Deficiency

MARY HARMON, M.D., Cleveland

Parathyroid adenomas are exceedingly rare in childhood. Primary hyperplasia of the parathyroid gland has been reported in infants and young children, but the parathyroid adenoma seems to be almost exclusively a disease of the older age group. Of 140 cases in a recent Mayo Clinic series, the youngest was 14 years old.[1] The case to be presented, at 7 years of age, represents the youngest child with a functioning adenoma, surgically removed and proved pathologically. It is the purpose of this report to review primary hyperparathyroidism as it is seen in children and to stress two unusual features of this case, namely, permanent neurological damage and an unusual serum magnesium deficit.

REPORT OF A CASE

A 6-year-old Negro boy was first admitted to the Cincinnati General Hospital on Nov. 11, 1953, with the following history. Five days prior to admission he was listless and complained of headache and aching extremities. These symptoms, which became increasingly severe during the next two days, were followed by persistent vomiting and generalized abdominal pain. The development of a painfully stiff neck and back precipitated his admission.

Ten months prior to admission, the patient was hospitalized in Alabama for "pneumonia." Four days later, at the time of discharge, his symptoms of fever, cough, and listlessness had cleared, but soon thereafter he began to complain of stiffness in his knees and a sensation of weakness in his legs, difficulties which intermittently progressed during the ensuing months. Despite an adequate intake of food, he had been losing weight for at least five months prior to admission. For the month preceding admission, the patient noted ill-defined pains in his arms and legs. Bowel habits were thought to be normal, and there were no urinary symptoms. Birth and development had been normal, and the past history and family history were noncontributory.

Physical examination on admission revealed an emaciated, dehydrated, irritable, and disoriented boy, weighing 36 lb. Temperature and pulse were normal, and the blood pressure was 100/50 mm. Hg. Vision seemed intact although difficult to evaluate, and the fundi were normal. The neck and back were rigid. There were a few shotty cervical lymph nodes palpable. The lung fields were clear to percussion and auscultation, and the heart was normal except for a soft Grade 1 systolic murmur along the lower left sternal border. The abdomen was distended and diffusely tender, and the stomach, in particular, was massively dilated; there was a large fecal impaction; bowel sounds were normal. The extremities appeared wasted equally, and although there was pain on movement of the major joints, there was no objective evidence of arthropathy, and bone tenderness was not elicited. The deep tendon reflexes were hyperactive but, aside from his sensoral changes, the remainder of the neurological examination was unremarkable.

Submitted for publication Sept. 21, 1955.

Trainee of the Institute of Arthritis and Metabolic Disease, United States Public Health Service, 1954-1955.

From the Department of Pediatrics, University of Cincinnati College of Medicine, and The Children's Hospital Research Foundation, Cincinnati.

Dr. Richard E. Goldsmith, of the Metabolism Laboratory, University of Cincinnati College of Medicine, gave valuable assistance in interpreting the metabolic data.

Routine laboratory data were as follows: the hemoglobin content was 12.0 gm. per 100 ml., and there were 15,500 leucocytes per cubic millimeter, 82% of which were neutrophiles. The urine specific gravity was 1.016; albumin and sugar were not present; the sediment contained 5-8 WBC per high-power field. A lumbar puncture produced clear cerebrospinal fluid, containing 45 mononuclear cells per cubic millimeter; the sugar content of this fluid was 85 mg. per 100 ml. and the protein, 44 mg. per 100 ml.; the Wassermann and gold-curve determinations were negative. Chemical findings in the serum were suggestive of mild dehydration and a mild metabolic alkalosis; in milliequivalents per liter the concentrations were as follows: chloride, 85; sodium, 140; potassium, 4.9; bicarbonate, 29. The blood urea nitrogen was 43 mg. per 100 ml.

The child remained disoriented and vomited persistently. There was a low-grade fever and urinary incontinence. On the basis of a strongly positive blood Kahn test, which has never reverted to normal, he was treated for 12 days with a total of 7,200,000 units of penicillin. No family history of syphilis could be obtained, and the mother and siblings were serologically negative.

On the fourth hospital day the patient sustained a grand mal convulsion, at which time he was found to be pulseless and apneic. Calcium gluconate and a barbiturate were given intravenously, and the pulse returned at a rate of 45 per minute. Chemistry values of blood drawn a few minutes after this episode showed a serum calcium of 6.0 mEq/liter and a serum inorganic phosphorus of 6.2 mEq/liter. An electrocardiogram substantiated the diagnosis of complete heart block, a finding which disappeared within one week. The post-seizure blood pressure was 154/98 mm. of Hg.

Subsequent urinalyses showed a specific gravity consistently below 1.010; a few WBC, RBC, and granular and hyaline casts were usually present, but there was no albuminuria. Later hemograms showed a hemoglobin content of between 9.0 and 13.0 gm. per 100 ml. and a white blood cell count that varied from 9900 to 23,500 per cubic millimeter, with a predominance of neutrophiles. B. U. N. and N. P. N. fell with hydration and remained thereafter within normal limits, the serum potassium fluctuated widely between 2.0 and 8.4 mEq/liter. One serum calcium of 8.5 mEq/liter and one serum inorganic phosphorus of 2.0 mEq/liter were recorded after the initial values. The C. S. F. mononuclears diminished, but the protein remained slightly elevated; the Wassermann test and gold curve were again negative.

A host of esoteric diagnoses were being considered at this time, including various encephalitides, Weil's disease, trichinosis, and the collagen group of diseases. Numerous laboratory studies failed to clarify the problem. The total protein was 7.5 gm. per 100 ml., of which 4.5 gm. was albumin and 3.5 gm. globulin. Liver-function tests were within normal limits except for a 3+ cephalin flocculation. Specific serum agglutinins for typhoid, paratyphoid, Brucella, Leptospira, etc. were run, but the titers were either negative or insignificant. Other negative studies included skin tests for tuberculosis, histoplasmosis, trichinosis, and brucellosis; repeated cultures of stool, blood, and bone marrow for bacteria, acid-fast bacilli, and fungi; L. E. cell and sickle-cell preparations; skin and muscle biopsies; and roentgenograms of the skull, abdomen, chest, and long bones.

Although the boy's clinical condition fluctuated, there was gradual improvement, so that, at the end of a month, he was able to sit in a chair, mentally alert and pain-free. He was then discharged, without a definite diagnosis, to the Children's Convalescent Home, where he resisted all attempts at mobilization. While there, his blood pressure ranged from 125/80 to 150/100 mm. of Hg, and on Dec. 23, 1953, vomiting suddenly recurred. On the following day he was found to be semistuporous and complaining of headache. He was transferred to the Cincinnati General Hospital Receiving Ward, where the physical findings were essentially those of the previous admission with the following exceptions: the boy's eyes were fixed in the midline, with pupils dilated and corneal reflexes absent; there was marked nuchal rigidity, and the abdominal reflexes could not be elicited; the blood pressure was 150/100 mm. of Hg. While the child awaited transfer to the ward, twitching developed in his right hand; this was followed by a severe generalized convulsion. Barbiturates and finally ether were necessary to control the seizure.

The hemogram and urinalysis were in the range of those previously described. The C. S. F. on this admission contained 68 mononuclear cells per cubic millimeter and 77 mg. of protein per 100 ml. As he cleared mentally, the child complained bitterly of pain in his arms and legs and refused to move; any manipulation produced screaming. His weight was 33 lb. and remained there despite attempts at high-calory tube feedings. Hypertension was now sustained, and some degree of fecal impaction was ever present. A fairly definite clinical pattern began to emerge. From periods of moderate well being, during which the child was alert and hungry, he would pass into a state of lethargy; persistent vomiting and fever would ensue, and finally coma and/or convulsions would supervene. The entire cycle, lasting approximately 10 days, repeated itself several times. The cellular response of the C. S. F. paralleled the child's clinical condition, but the protein content steadily rose to reach a level of nearly 100 mg. per 100 ml. Unfortunately, there were insufficient calcium determinations obtained during this

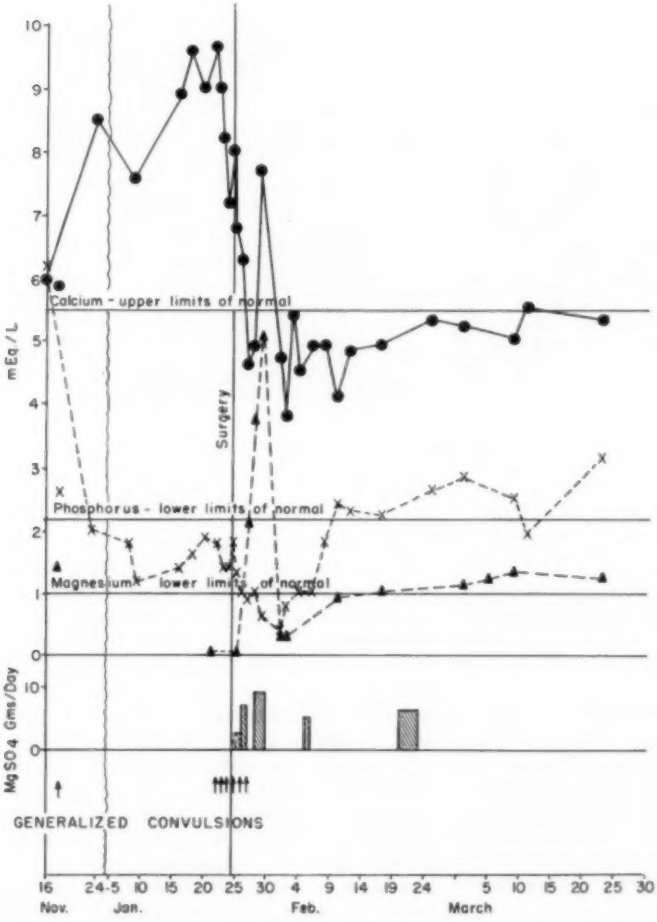

mEq/L
Calcium - upper limits of normal
Surgery
Phosphorus - lower limits of normal
Magnesium - lower limits of normal
MgSO4 Gms/Day
GENERALIZED CONVULSIONS
16 24-5 10 15 20 25 30 4 9 14 19 24 5 10 15 20 25 30
Nov. Jan. Feb. March

Fig. 1.—Serum concentrations of calcium, phosphorus, and magnesium, in mEq/liter. The number of grams of parenteral magnesium sulfate administered and the occurrence of convulsions are also depicted.

period to attempt to correlate the above symptoms with changes in the serum calcium concentration. Toward the end of December it became obvious that the boy was blind. His pupils were noted to react sluggishly to light, but the fundi were still normal. Electroencephalography showed a right temporal dysrhythmia, and the record was not altered by illuminating the eyes. A diagnosis of diffuse cortical blindness was made. Shortly thereafter, he developed permanent spasticity of both legs and the right arm.

In January, 1954, investigation of the child as a patient with a metabolic disorder was first begun. Laboratory evidence of parathyroid disease, in addition to the two previous high serum calcium values, was rapidly accumulated. These data appear graphically in Figures 1 and 2. There was a persistently elevated serum calcium together with a depressed serum phosphorus, a slightly elevated serum alkaline phosphatase, and an increased urinary excretion of calcium on a calcium intake of less than 0.3 gm. per day. A profusion of osteoblasts on bone marrow smears was additional evidence of metabolic bone disease (Fig. 3).

A routine roentgenographic survey for metabolic bone disease demonstrated a generalized and severe degree of osseous demineralization. The epiphyseal areas showed no additional abnormalities, except for nebulous calcific deposits in the hyaline cartilage of many of the secondary centers of ossification. In the skull, the teeth, which were normal in density, offered a striking contrast to the decalcified bones, which had a homogeneous, glassy appearance. The lamina dura were absent or markedly deficient. Ocular calcification was not visualized. The soft tissues of the extremities were atrophic, but ectopic calcification was not present. The long bones were coarsely trabeculated and the cortices thinned. In the metaphyseal regions of the proximal tibia and

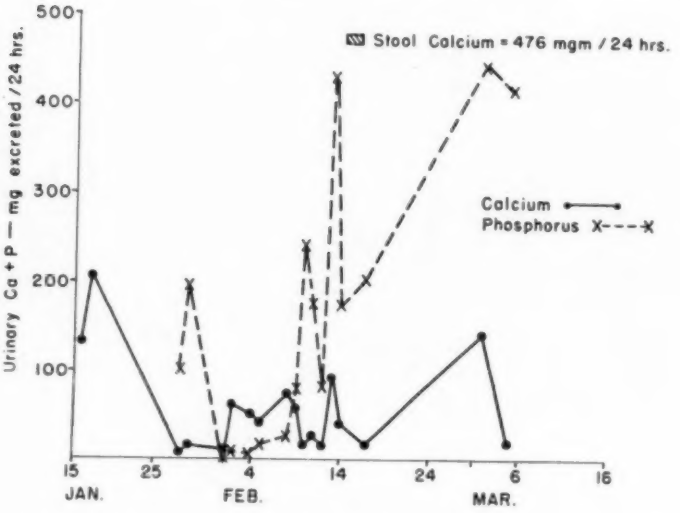


Fig. 2.—The calcium and phosphorus content of 24-hour urine collections. The preoperative values were obtained while the patient was receiving less than 0.3 mg. of calcium per day. (Some of these figures are questionable because of collecting difficulties.)

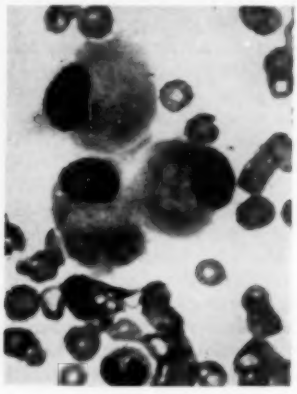
in the distal radius, the normal sharply defined, external edges had been replaced by a fuzzy border caused by subperiosteal resorption (Figs. 4 and 5). Intravenous urogram: a small calculus was present in the left kidney, but the urinary tract was otherwise normal. No tumor in the neck could be visualized during barium swallow.

A diagnosis of hyperparathyroidism was made.

The patient's condition deteriorated to a desperate state; he was semistuporous, and there was constant twitching of his extremities. On the evening prior to surgery, intravenous edathamil disodium (Disodium Versenate),* a chelating agent, was administered in hopes of diminishing his serum calcium concentration and possibly his symptoms of severe calcium intoxication. While he was receiving the drug, the child's blood pressure rose from 185/140 to 220/180 mm. of Hg. He became extremely restless and screamed with abdominal pain. The drug was discontinued after less than half of the calculated dose of 30 mg. per pound had been given. During this period, the serum calcium fell from 9.6 to 9.0 mEq/liter. Twitching was not observed thereafter, and the blood pressure fell to 130/90 mm. of Hg.

* Supplied by Riker Laboratories, Inc.

Fig. 3.—Photomicrograph of bone marrow smear which shows the presence of osteoblasts; × 1400.



On Jan. 24, 1954, the child's neck was explored. Behind and displacing the right lobe of the thyroid a 2.5×1.0 cm. smooth oval mass was encountered. When this was excised it was found to be pinkish-gray, firm, and encapsulated. Although in the gross it was not thought to be characteristic of parathyroid tumor, a frozen section indicated that this was indeed the case. There was no obvious invasion of the capsule, and the regional lymph nodes were not enlarged. Small pieces of two other structures thought to represent atrophic parathyroid glands were removed for biopsy; in each instance microscopic examination showed adipose tissue. Sections of the parathyroid adenoma revealed an unusual and varied pattern (Fig. 6). The lesion was devoid of fat and consisted of closely packed epithelial cells, the margins of which were sharply defined. Cells ranged in diameter from 10μ to 20μ and contained abundant cytoplasm, which in some instances was opaque and amphophilic and in others clear and unstained. The latter were identical with the secretory "wasserhelle" cells peculiar to the parathyroid. Nuclei were pleomorphic and often bizarre in configuration. In the main, these were filled homogeneously with chromatin but occasionally assumed a variable structure. Occasional mitotic figures were

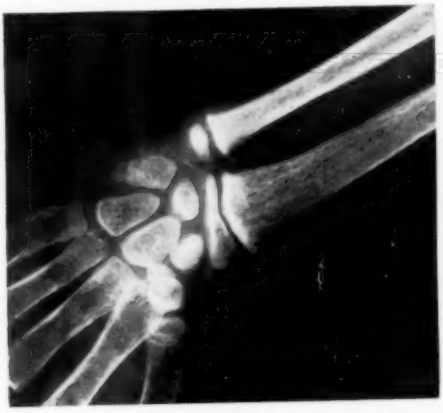


Fig. 4.—Roentgenogram of the left forearm, illustrating diffuse demineralization and calcification of the hyaline cartilage.

Fig. 5.—Roentgenogram of upper incisors in which the lamina dura cannot be identified.

encountered. There was no evidence of intravascular or capsular invasion. Because of the peculiar histologic structure, the lesion was submitted to Dr. Benjamin Castleman, Boston, for consultative opinion. It was his belief that it represented an unusual, but nonetheless benign, parathyroid adenoma. A small amount of the non-neoplastic gland included in the specimen showed atrophy, indicating that this was indeed a hyperfunctioning neoplasm and not a form of primary hyperplasia. The operation was uneventful, except for laryngospasm which developed immediately postoperatively and necessitated emergency tracheotomy.

During the first 36 postoperative hours the boy was hypertensive and semicomatose and demonstrated constant twitching of all his extremities. At this point, the following serum values were obtained: calcium, 6.8 mEq/liter; potassium, 2.4 mEq/liter; and magnesium, 0.17 mEq/liter. Magnesium determinations were being done on a research basis, and there was a delay in the report; therefore, the preoperative and postoperative serum magnesium values were reported simultaneously; both were less than 0.2 mEq/liter. $MgSO_4$ and KCl were administered with prompt marked clinical improvement (Fig. 1). Although the blood pressure fell, it never reached normal values. During the next few days the child was alternately alert and stuporous, and there were occasional muscle twitchings. Generalized convulsions, however, were not observed after the third postoperative day. On the 12th postoperative day a serum magnesium value of 0.33 mEq/liter from four days previously was reported. This was one week after discontinuance of intramuscular $MgSO_4$. The child had been restless and sweating, but after $MgSO_4$ was again admin-

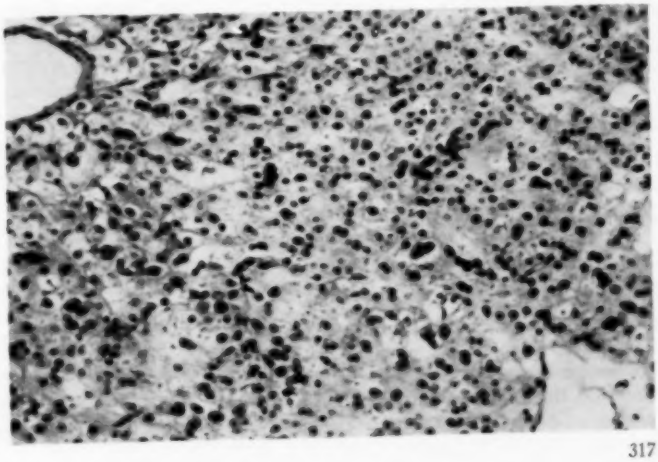


Fig. 6.— Photomicrograph of section of parathyroid adenoma.

istered he became much more alert and was able to sit up in a chair for the first time. At no time was there clinical evidence of true tetany, even on the 10th postoperative day when the serum calcium was as low as 3.8 mEq/liter. Subsequent calcium values were all within normal limits, probably maintained by the varying amounts of $CaCl_2$, vitamin D, and even a short trial of dihydrotachysterol (A. T. 10), which he had received since surgery. During the first 14 postoperative days the serum phosphorus concentration remained below preoperative values, first becoming normal on the 17th postoperative day. Oral phosphorus was given as NaH_2PO_4 during part of this period because of the known interrelation of phosphorus and magnesium with essential enzyme systems. After the first two postoperative weeks a sustained clinical improvement could be seen. The patient began to gain weight and mental alertness. There was no progression of his neurological disease, and the spinal fluid protein content gradually returned to normal. However, the lesions present at the time of surgery did not improve. The boy remained blind and spastic and developed contractures severe enough to require orthopedic correction. Subsequent electroencephalograms showed a progression of a diffusely disordered pattern. The blood Kahn, Wassermann, and syphilis complement fixation tests remained strongly positive after a second course of penicillin, and it was decided that, aside from serological evidence, there was little to suggest syphilis. The relationship of his abnormal serology to his primary disease remains obscure.

In March, 1954, renal function studies were first performed (Table). There was reduced ability to

Renal Function Studies

1. Urinary concentration test
   Overnight..581 mOsm. per liter: 12 hr. without liquids
   U-1.....677 mOsm. per liter: 13 hr. without liquids
   U-2.....566 mOsm. per liter: 14 hr. without liquids
   (Normal: 1,000-1,100 mOsm. per liter)
2. Glomerular filtration rate (inulin clearance)
   72.6 ml./min./1.73 sq. m.
   (Normal: 120 ml./min./1.73 sq. m.)
3. Maximal tubular reabsorption mass (Tm_{PAH}) (*p*-aminohippurate)
   41.6 mg./min./1.73 sq. m.
   (Normal: 77 mg./min./1.73 sq. m.)

concentrate urine, reduced glomerular filtration rate, and reduced maximal tubular mass as determined with *p*-aminohippuric acid; all are indicative of a generalized renal impairment, consistent with a diagnosis of nephrocalcinosis. In April there was x-ray evidence of moderate remineralization of the bones and the lamina dura. The boy has never been completely mobilized however, and some sustained demineralization was to be expected. In June, 1955, the skeletal system appeared roentgenographically normal except for persistent calcific deposits in the hyaline cartilages. Of particular interest at that time was the comparable density of the teeth and skull.

The child remains blind and spastic. Although moderately intelligent, he has become a definite behavior problem, illustrated by fits of rage and hyperactivity. The blood pressure has stabilized at 130/90 mm. of Hg. Routine urinalyses and serum calcium, phosphorus, magnesium, and alkaline phosphatase values have all remained within normal limits.

COMMENT

General Features of Primary Hyperparathyroidism

In the few detailed reports of primary hyperparathyroidism in children, the disease seems to conform, in most respects, to the following clinical classification:

1. Symptoms due to skeletal disease
2. Symptoms due to renal disease
3. Symptoms due to hypercalcemia and parathyroid hormone "intoxication"
4. A combination of the above

Practically all of the well-known symptoms were obvious at some stage of the present patient's illness.

In this case, symptoms of bone disease were very much in evidence. While bone pain may be the only clinical manifestation of skeletal involvement, there may be pathological fractures and bending deformities. Roentgenographically, generalized demineralization and absent lamina dura are important points in establishing the diagnosis, but in addition there may be ectopic soft-tissue calcification and areas of osteitis fibrosa cystica.

According to Albright and Reifenstein,[2] the demineralization of the skeleton is a secondary effect of the parathyroid hormone, the primary action of which is on the renal tubules. Administration of parathyroid hormone to nephrectomized animals also causes demineralization of the skeleton[3] and increased serum calcium levels.[4] It therefore seems possible that the hormone acts directly on the skeleton as well as the kidneys.

The polyuria of early hyperparathyroidism is an osmotic diuresis due to increased urinary excretion of phosphate and calcium. Associated with the osmotic diuresis is a diminished concentrating ability of the kidneys, as revealed by specific gravity of freezing point depression tests in morning urines.

Irreversible renal damage might later ensue, due to nephrocalcinosis, with or without renal calculi.[1] In our case, renal function tests performed after operation showed evidence of irreversible damage, such as lowered glomerular filtration rate, Tm_{PAH}, and concentrating ability.

The increased phosphate excretion is, according to Albright's theory, due to a direct action of parathyroid hormone on the kidneys. A number of investigators within recent years have shown that this hormone depresses the Tm for phosphate reabsorption.[5] The loss of phosphate in the urine results in low plasma levels of phosphate; consequently calcium is mobilized from the skeleton and in turn also floods the urine, as it exceeds the reabsorptive calcium Tm.

As renal insufficiency with lowered glomerular filtration rate later ensues, the plasma level of phosphate returns to normal or higher levels. Azotemia, therefore, is a common finding and hypertension a likely sequel to renal damage. Even in cases with minimal renal involvement, kidney function often remains suboptimal after the adenoma has been removed and a normal calcium level reestablished.

The term "parathyroid hormone intoxication" implies a severely toxic state associated with acute renal failure and a high mortality rate. Shelling and co-workers [6] ascribed this syndrome to dehydration caused by the diuretic action of the hormone and advocated the use of intravenous saline as a life-saving measure. Hanes [7] believed that parathyroid hormone in massive doses caused tissue necrosis, which in turn led to the widespread calcification often found when these cases come to necropsy. Albright and Reifenstein [2] and Howard and co-workers [8] believe that at a critical concentration of calcium in the extracellular fluid, about 9 mEq/liter, the kidney no longer clears phosphate normally and there results a phosphate retention leading to supersaturation of the extracellular fluid in terms of calcium phosphate. Ectopic deposition of this material then occurs, and chemical death may ensue. Grollman [9] and Hopkins and co-workers [10] have presented data to support this theory. When the patient reported above appeared most dangerously ill, with a serum calcium approaching 10 mEq/liter, saline was administered without obvious benefit. Because of its calcium-binding properties, edathamil disodium was given. The results of this therapy could not be evaluated, owing to the patient's alarming hypertensive response, a reaction paradoxical to the drug's known hypotensive properties. Lowe and co-workers [11] administered oral edathamil (EDTA) to a child with idiopathic hypercalcemia without producing an appreciable change in the serum calcium level. In summary, we believe that parathyroid hormone "intoxication" was suggested in our case by recurrent transient episodes of vomiting, fever, mental confusion and convulsions, and the very high serum calcium.

It is important to recognize early nonspecific symptoms and signs if permanent damage is to be prevented. Fever and leucocytosis, prominent in this case, may divert the clinician's thinking to infectious rather than metabolic disease. The fever is often striking † but has not been stressed in the literature. In any case of hyperparathyroidism, gastrointestinal disturbances may dominate the clinical picture, as described in the report of a 13-year-old girl with a parathyroid adenoma who died of paralytic ileus.[14] Anorexia, vomiting, difficulty in swallowing, and constipation of some degree are the rule. An interesting but poorly understood phenomenon is the association of peptic ulceration with hyperparathyroidism, which has often been noted in adults but which has not as yet been described in children.

Laboratory Data Helpful in the Diagnosis of Hyperparathyroidism

Routine laboratory examinations will yield little information of differential diagnostic significance. The hemogram varies, but a mild anemia is often present. There may be a leucopenia as a result of myelofibrosis or

† References 12 and 13.

a leucocytosis, as in this case, perhaps on the basis of tissue necrosis. The results of routine urinalysis will depend on the degree of renal involvement. In the case reported above, the strongly positive serological test for syphilis remains a puzzle. There were no other obvious alterations in the child's immune-body mechanism and no reason, other than the serological findings, to believe he had syphilis. No similar case, with a false positive serology complicating hyperparathyroidism, can be found in the literature.

Specific confirmation of the diagnosis of hyperparathyroidism is found only in the serum and urine chemistry studies. Classically, there should be hypercalcemia and hypophosphatemia, but this combination is not inviolable. There are many cases now reported in which the serum calcium barely exceeds 5 mEq/liter. The 9 mEq/liter, as observed in this case, is unusually high, and, while higher values have been recorded, most such cases have ended fatally.‡ Hypophosphatemia is a more constant finding than hypercalcemia, but the concentration of phosphorus in the serum depends on renal sufficiency and may be normal or even above normal if renal decompensation has occurred. The serum alkaline phosphatase, which reflects osteoblastic activity (Fig. 5) and therefore the severity of bone disease, need not be elevated if the bones are normal. Additional data of differential diagnostic significance can be obtained by measuring the calcium content of several 24-hour urine specimens after the patient has been placed on a low-calcium diet for at least three days. While receiving less than 0.3 gm. of calcium per day, the patient excreted 133 and 208 mg. of calcium per 24 hours. In our laboratory this is considered elevated for a child of this age, particularly for a child with demineralized bones, who should excrete less than the usual amounts of calcium. A renal calculus is further presumptive evidence of hypercalcuria.

Chemically, the postoperative course was typical for this disease (Figs. 1 and 2). The serum calcium rapidly fell, reaching a low of 3.8 mEq/liter by the seventh postoperative day and returning to normal levels thereafter. Continuous parenteral and later oral calcium prevented the development of tetany and lower calcium levels. Urine losses were minimal, as apparently were those in the stool. The serum inorganic phosphorus, already low, was even further depressed at a time when urinary phosphate excretion was minimal. The best explanation for this phenomenon is that there was considerable redeposition of calcium and phosphorus in the child's demineralized bones. Normal phosphorus values in serum and urine were reached by the third postoperative week.

The Association of Central Nervous System Abnormalities with Hyperparathyroidism

The most striking symptoms and signs in the case presented above involved the nervous system. Their bizarre character and severity delayed the correct diagnosis for several weeks, and this delay resulted in a child with permanently disabling neurological problems. The central nervous system changes were apparently widespread, involving at least the first order optic neurons and areas of the pyramidal system. It seems quite likely that hyperparathyroidism was primarily responsible for these changes. Crises occurred at regular intervals, during which lethargy progressed to convulsions or coma and during which a cerebrospinal fluid pleocytosis was superimposed on a steadily mounting cerebrospinal fluid protein. There have been very few reported examinations of the cerebrospinal fluid in hyperparathyroidism, and these have been normal, unlike the results in the present case.§ Unfortunately, too few serum calcium determinations were obtained early in this patient's course to try to correlate the level of hypercalcemia with the severity of symptoms.

Recently it has been reported that mental and minor neurological difficulties, as summarized by Bartter,[20] are frequently associated with hyperparathyroidism in adults. Neurotic or psychotic complaints may be the

‡ References 15-17.

§ References 18 and 19.

presenting or dominant symptoms [18] and seem to be particularly common in cases of peptic ulceration associated with hyperparathyroidism.‖ In cases of "parathyroid hormone intoxication," mental or neurological aberrations are consistently present and may include disorientation, convulsions, and coma.¶ In children, the incidence of neurological involvement is not marked but, when present, may be severe enough to dominate the clinical picture.

Anspach and Clifton [24] reported two cases strikingly similar to the subject of this report. One was an 11-year-old girl who presented with fractures, fever, convulsions, and vomiting. Two years later, progressive mental deterioration was noted, and, although a parathyroid tumor was removed after further delay, convulsions continued and contractures developed. The highest serum calcium concentration noted was 8.3 mEq/liter; the blood pressure was not recorded. The second case # was only 3 months of age when weight loss, polyuria, and bone tenderness were first observed. When hyperparathyroidism was suspected two years later, optic atrophy and mental retardation were present. The highest serum calcium value was 8.1 mEq/liter; renal function was thought to be normal; the blood pressure was not given. Although the child improved after the neck was irradiated, no parathyroid disease was ever proved. In 1928, Duken [25] reported a case of a 7-year-old girl who was cachectic and sustained convulsions as a result of the disease. A 10-month-old infant with idiopathic hyperplasia of the parathyroids and a serum calcium of 11.1 mEq/liter was mentally and physically retarded.

When a patient with a parathyroid adenoma has repeated convulsions or blindness, the fascinating syndrome of multiple endocrine adenomas should be considered. Over half of the patients with this condition in the Mayo Clinic series have had single or multiple islet-cell tumors.* Blood-sugar determinations in the case reported above were normal.

Undoubtedly, no single factor can be incriminated for the neurological and mental symptoms associated with hyperparathyroidism; however, certain obvious possibilities immediately come to mind. Uremia, which must be ruled out, was not present in our case. Hypertensive encephalopathy, as Ford [27] defines the syndrome in childhood, includes a multiplicity of bizarre symptoms, many of which were observed in the patient presented above. However, papilledema, hypertensive retinopathy, and an elevated cerebrospinal fluid pressure were lacking, as was a significant degree of hypertension during the first convulsive episode. Also to be considered are vascular spasm and hemorrhage in multiple small cerebral vessels, but the unusual distribution and permanency of the lesions, together with the degree of pleocytosis and protein elevation in the cerebrospinal fluid, point toward some other etiological agent.

The general effect of massive doses of parathyroid hormone have been discussed previously. Collip [23] produced psychic depression in animals receiving an overdose of parathyroid hormone. These results were inadvertently verified in the case of a 5-year-old boy who received massive doses of the hormone and who developed vomiting, lethargy, and mental confusion.[12]

But most authors favor the theory that severe hypercalcemia with the deposition of insoluble calcium phosphate salts in the brain and other tissues is the mechanism of disaster in parathyroid hormone overdosage.[18] There are enough reported cases of neurological damage following the hypercalcemia of vitamin D "intoxication,"† of the immobilization syndrome,‡ and of idiopathic hypercalcemia [11] where parathyroid hormone is supposedly not in excess, to substantiate this idea. A de-

‖ References 13, 21, and 22.

¶ References 7, 12, 19, and 23.

Since this paper was submitted it has been brought to my attention that this case was in reality one of hypophosphaturia. It will be reported at a later date by Dr. Edna Sobel.

* References 1 and 26.

† References 28 and 29.

‡ References 30 and 31.

myelinating or fibrosing type of cerebral disease, secondary to the deposition of calcium phosphate or to the hypercalcemia per se, is also a possibility.

Finally, the neurological sequela resulting from the depletion of body magnesium is an attractive but poorly explored area. The possible relationship to the present case will be discussed in the following paragraphs.

Magnesium Metabolism

Normal values for serum magnesium § lie somewhere between 1.4 and 2.6 mEq/liter.‖ The concentration of this ion in the intracellular fluid is approximately 25 times that in the interstitial fluid.[36] Like potassium, serum values inadequately reflect available body stores and losses are not rapidly replaced. The various functions of magnesium in general metabolism are poorly understood, but its presence is necessary for such processes as the formation of bone salts; the functioning of essential enzyme systems, including those regulating the synthesis of both protein and carbohydrate; and the maintenance of normal neuromuscular conductivity.

The symptoms of magnesium deprivation in rats were first described by Krause, Orent, and McCollum [37] as a form of tetany distinguished from hypocalcemic tetany by intense vasodilatation. Tufts and Greenburg ¶ verified these observations and showed that the early phase of hyperemia and hyperexcitability was followed by marked malnutrition, cachexia, dermatitis, edema, and degenerative changes in the heart and kidneys. The renal lesions were of particular interest in that progressive calcification of the corticomedullary zone and the cortex followed prolonged magnesium deprivation in the rat,[40] and similar changes were later observed in the rabbit.[41]

There is evidence that magnesium acts on the motor nerve terminals and directly on muscle fibers,[42] as well as on the central nervous system.# The hyperexcitability which appears early in the magnesium-deficiency syndrome is probably a reversible process, but Bird [45] has described cerebellar degeneration in chicks on a magnesium-deficient diet, and Barron and co-workers [41] were able to reproduce these results in rats and rabbits.

The relationship of magnesium to calcium appears to be an intimate one. The urinary and fecal excretion is increased by the parenteral administration of calcium chloride [46] and by parathyroid hormone.* Calcium ions will restore irritability to magnesium-narcotized neuromuscular tissue,† and when excess calcium is given to magnesium-deficient animals, hyperirritability and growth retardation appear earlier and are severer.[50] Diets high in potassium or protein have a similar aggravating effect on the magnesium-deficiency syndrome in the rat.‡ The latter observation would explain the spontaneous magnesium deficiency in cattle known as "grass tetany," which may develop in animals feeding on protein-rich spring grass.[52]

Clinically, alterations in magnesium metabolism are more difficult to evaluate. Since magnesium is an important intracellular component, it is not surprising to find changes in serum megnesium concentration paralleling those of potassium. In cases of acute renal failure, Martin and co-workers [36] demonstrated a rising serum magnesium which fell to levels below normal during the diuretic phase. Similar changes were observed in patients recovering from diabetic coma, and the authors hypothesized that magnesium, together with potassium, shifted back into the cells as glycogenesis was restored. Although some serum values were as low as 0.6 mEq/liter, the patients remained asymptomatic. Flink and associates,[35] however, stress the fact that body stores must be exhausted before symptoms appear. They repeatedly demonstrated a significantly low

§ Magnesium was determined by a modification of the methods of Drosdoff and Nearpass [32] and Orange and Rhein.[33]

‖ References 34-36.

¶ References 38 and 39.

References 43 and 44.

* References 47-49.

† References 44 and 45.

‡ References 50 and 51.

serum magnesium in patients with chronic alcoholism complicated by delirium tremens, many of whom were markedly improved by the parenteral administration of magnesium sulfate. A similar syndrome consisting of bizarre, involuntary muscular activity, followed in some cases by convulsions and delirium, was observed in postoperative patients receiving prolonged magnesium-free parenteral fluid therapy. Miller[53] reported the case of a 6-year-old boy who had had intermittent convulsions and twitching since early infancy. The only alteration in the serum chemistry values was a magnesium concentration as low as 0.5 mEq/liter, and when magnesium sulfate was administered there was a striking alleviation of symptoms.

It is more difficult to correlate the clinical and experimental data relating calcium to magnesium metabolism. Theoretically, parallel serum concentrations should be expected and have been observed in cases of hyperparathyroidism, hypoparathyroidism, and neonatal tetany.§ (Hypocalcemia has always been considered the sole cause of hyperirritability in these cases of hypoparathyroidism and tetany.)

On the other hand, hypomagnesemia has been reported in association with hypercalcemic states. In the idiopathic hypercalcemia of infancy, serum magnesium values have been noted which were significantly low.‖ Two cases of fracture with nonunion were associated with hypomagnesemia.[54] In a report by Bulger and Gausmann,[49] a patient with hyperparathyroidism was found to be in negative magnesium balance, which became positive after surgical removal of her adenoma. Analysis of these data suggests that magnesium had been lost as a magnesium phosphate salt in excess of the ratio of magnesium to phosphorus predicted for normal bone.

Perhaps the initial response of magnesium to stimuli, such as parathyroid hormone, which produce hypercalcemia, is hypermagnesemia. Increased excretion of magnesium and subsequent depletion of body stores may then ensue. If, in the case presented in this report, a total body magnesium deficit existed, many of the child's signs and symptoms could be explained on this basis. The extremely low serum magnesium concentration; the muscular tremors, convulsions, and coma; the permanent neurological lesions; the cachexia and malnutrition, all possibly aggravated by hypercalcemia and high-protein tube feedings and favorably responding to magnesium sulfate therapy, are consistent with the magnesium-deficiency syndrome. Finally, although nephrocalcinosis is classically associated with hypercalcemia and hypercalcuria, there is an interesting possibility that the magnesium deficiency contributed to the total degree of renal damage.

SUMMARY AND CONCLUSIONS

A case of hyperparathyroidism in a young boy is presented. Because of the rarity of parathyroid adenomas in childhood, the general features of the disease are discussed, stressing the symptoms related to the central nervous system which may be commoner, especially in childhood, than has been recognized previously. The pathogenesis of the neurological damage in this case is unknown, but prolonged and extreme elevations of calcium and depletion of magnesium, as reflected in the serum concentrations, are intriguing etiological possibilities. The cause and effects of the magnesium deficit are considered, but further study of this ion in hyperparathyroidism is needed, not only in relation to calcium metabolism, but also in relation to the other intracellular and extracellular electrolytes.

Dr. Emanuel Levin, of the University of Cincinnati College of Medicine, interpreted the roentgenograms, and Dr. Edward Gall, also of the University of Cincinnati, made the report of the pathology of the adenoma. Dr. Gall and Dr. Marshall Lee, who performed the surgery, included this case in a group presented before the Southern Surgical Society, in 1954. Drs. Clark West and George Guest, of the Children's Hospital Research Foundation, did the renal function studies and the magnesium determinations, respectively.

1993 Laurel Hill Dr. (21).

§ References 55-57.

‖ References 11 and 58.

REFERENCES

1. Black, B. M.: Hyperparathyroidism, Springfield, Ill., Charles C Thomas, Publisher, 1954.

2. Albright, F., and Reifenstein, E. C., Jr.: The Parathyroid Glands and Metabolic Bone Disease: Selected Studies, Baltimore, Williams & Wilkins Company, 1948.

3. Selye, H.: Mechanism of Parathyroid Hormone Action, Arch. Path. **34**:624, 1942.

4. Stewart, G. S., and Bowen, H. F.: The Parathyroid Control of Serum Calcium Independent of Renal Mediation, Endocrinology **48**:568, 1951.

5. Bartter, F. C.: The Parathyroids, Ann. Rev. Physiol. **16**:429, 1954.

6. Shelling, D. H.; Kajdi, L., and Guth, L.: Calcium and Phosphorus Studies: Effect of Repeated Doses of Parathyroid Extract on the Chemical Composition of the Blood and Urine of the Dog; Explanation of the Cause of Death in Parathyroid Overdosage, Endocrinology **22**:225, 1938.

7. Hanes, F. M.: Hyperparathyroidism Due to Parathyroid Adenoma with Death from Parathormone Intoxication, Am. J. M. Sc. **197**:85, 1939.

8. Howard, J. E.; Follis, R. H., Jr.; Yendt, E. R., and Connor, T. B.: Hyperparathyroidism: Case Report, J. Clin. Endocrinol. **13**:997, 1953.

9. Grollman, A. J.: The Condition of the Inorganic Phosphorus of the Blood with Special Reference to the Calcium Concentration, J. Biol. Chem. **72**:565, 1927.

10. Hopkins, T.; Howard, J. E., and Eisenberg, H.: Ultrafiltration Studies on Calcium and Phosphorus in Human Serum, Bull. Johns Hopkins Hosp. **91**:1, 1952.

11. Lowe, K. G.; Henderson, J. L.; Park, W. W., and McGreal, D. A.: Idiopathic Hypercalcæmic Syndromes of Infancy, Lancet **2**:101, 1954.

12. Lowenburg, H., and Ginsberg, T. M.: Acute Hypercalcemia: Report of a Case, J. A. M. A. **99**: 1166, 1932.

13. Rogers, H. M.: Parathyroid Adenoma and Hypertrophy of the Parathyroid Glands, J. A. M. A. **130**:22, 1946.

14. Arlt, H. G., and Asang, E.: Intestinaler Hyperparathyreoidismus, Ztschr. Kinderh. **73**:294, 1953.

15. Philips, R. N.: Primary Diffuse Parathyroid Hyperplasia in an Infant of 4 Months, Pediatrics **2**:428, 1948.

16. Pratt, E. L.; Geren, B. B., and Neuhauser, E. B. D.: Hypercalcemia and Idiopathic Hyperplasia of the Parathyroid Glands in an Infant, J. Pediat. **30**:388, 1947.

17. Smith, F. G., and Cooke, R. T.: Acute Fatal Hyperparathyroidism, Lancet **2**:650, 1940.

18. Fitz, T. E., and Hallam, B. L.: Mental Changes Associated with Hyperparathyroidism: Report of 2 Cases, A. M. A. Arch. Int. Med. **89**: 547, 1952.

19. Oliver, W. A.: Acute Hyperparathyroidism, Lancet **2**:240, 1939.

20. Bartter, F. C.: The Parathyroid Gland and Its Relationship to Diseases of the Nervous System, in Merritt, H. H., and Hare, C. C., Editors: Metabolic and Toxic Diseases of the Nervous System: Proceedings of the Association, December 12 and 13, 1952, New York, N. Y., Research Publications, Association for Research in Nervous and Mental Disease, Baltimore, Williams & Wilkins Company, 1953, Vol. 32, p. 1.

21. Rogers, H. M.; Keating, F. R., Jr.; Morlock, C. G., and Barker, N. W.: Primary Hypertrophy and Hyperplasia of the Parathyroid Glands Associated with Duodenal Ulcer: Report of an Additional Case, with Special Reference to Metabolic, Gastrointestinal and Vascular Manifestations, Arch. Int. Med. **79**:307, 1947.

22. Waife, S. O.: Parathyrotoxicosis: The Syndrome of Acute Hyperparathyroidism, Am. J. M. Sc. **218**:624, 1949.

23. Collip, J. B.: The Parathyroid Glands, Medicine **5**:1, 1926.

24. Anspach, W. E., and Clifton, W. M.: Hyperparathyroidism in Children: Report of 2 Cases, Am. J. Dis. Child. **58**:540, 1939.

25. Duken, J.: Beitrag zur Kenntnis der malacischen Erkrankungen des Kindlichen Skelettsystems: Spätrachitis und Osteodystrophia fibrosa, Ztschr. Kinderh. **46**:114, 1928.

26. Underdahl, L. O.; Woolner, L. B., and Black, B. M.: Multiple Endocrine Adenomas: Report of 8 Cases in Which the Parathyroids, Pituitary and Pancreatic Islets Were Involved, J. Clin. Endocrinol. **13**:20, 1953.

27. Ford, F. R.: Diseases of the Nervous System in Infancy, Childhood and Adolescence, Ed. 3, Springfield, Ill., Charles C Thomas, Publisher, 1952.

28. Chaplin, H., Jr.; Clark, L. D., and Ropes, M. W.: Vitamin D Intoxication, Am. J. M. Sc. **221**:369, 1951.

29. Ross, S. G., and Williams, W. E.: Vitamin D Intoxication in Infancy, Am. J. Dis. Child. **58**: 666, 1939.

30. Albright, F.; Burnett, C. H.; Cope, O., and Parsons, W.: Acute Atrophy of Bone (Osteoporosis) Simulating Hyperparathyroidism, J. Clin. Endocrinol. **1**:711, 1941.

31. Dodd, K.; Graubarth, H., and Rapoport, S.: Hypercalcemia, Nephropathy and Encephalopathy Following Immobilization: Case Report, Pediatrics **6**:124, 1950.

32. Drosdoff, M., and Nearpass, D. C.: Qualitative Microdetermination of Magnesium in Plant Tissues and Soil Extracts, Analyt. Chem. **20**:673, 1948.

33. Orange, M., and Rhein, H. C.: Microestimation of Magnesium in Body Fluids, J. Biol. Chem. **189**:379, 1951.

34. Haury, V. G., and Cantarow, A.: Variations of Serum Magnesium in 52 Normal and 440 Pathologic Patients, J. Lab. & Clin. Med. **27**:616, 1942.

35. Flink, E. B.; Stutzman, F. L.; Anderson, A. R.; Konig, T., and Frazer, R.: Magnesium Deficiency After Prolonged Parenteral Fluid Administration and After Chronic Alcoholism Complicated by Delirium Tremens, J. Lab. & Clin. Med. **43**:169, 1954.

36. Martin, H. E.; Mehl, J. W., and Wertman, M.: Symposium on Recent Advances in Medicine: Clinical Studies of Magnesium Metabolism, M. Clin. North America **36**:1157, 1952.

37. Krause, H. D.; Orent, E. R., and McCollum, E. V.: Studies on Magnesium Deficiency in Animals: I. Symptomatology Resulting from Magnesium Deprivation, J. Biol. Chem. **96**:519, 1932.

38. Greenburg, D. M.; Anderson, C. E., and Tufts, E. V.: Pathological Changes in the Tissues of Rats Reared on Diets Low in Magnesium, J. Biol. Chem. **114**:43, 1936.

39. Tufts, E. V., and Greenburg, D. M.: The Biochemistry of Magnesium Deficiency: I. Chemical Changes Resulting from Magnesium Deprivation, J. Biol. Chem. **122**:693, 1938.

40. Greenburg, D. M.; Lucia, S. P., and Tufts, E. V.: The Effect of Magnesium Deprivation on Renal Function, Am. J. Physiol. **121**:424, 1938.

41. Barron, G. P.; Brown, S. O., and Pearson, P. B.: Histological Manifestations of a Magnesium Deficiency in the Rat and Rabbit, Proc. Soc. Exper. Biol. & Med. **70**:220, 1949.

42. DelCastillo, J., and Engbach, L.: The Nature of the Neuromuscular Block Produced by Magnesium, J. Physiol. **124**:370, 1954.

43. Bryant, G. W.; Lehmann, G., and Knoefel, P. K.: Action of Magnesium on the Central Nervous System and Its Antagonism by Calcium, J. Pharmacol. & Exper. Therap. **65**:318, 1939.

44. Greenburg, D. M., and Tufts, E. V.: The Nature of Magnesium Tetany, Am. J. Physiol. **121**:416, 1938.

45. Bird, F. H.: Magnesium Supplementation in Relation to a Previously Reported Cerebellar Disorder in Chicks, Poultry Sc. **25**:396, 1946.

46. Mendel, L. B., and Benedict, S. R.: The Paths of Excretion for Inorganic Compounds: IV. The Excretion of Magnesium; V. The Excretion of Calcium, Am. J. Physiol. **25**:1; 24, 1909.

47. Greenwald, I., and Gross, J.: The Effects of the Administration of a Potent Parathyroid Extract upon the Excretion of Nitrogen, Phosphorus, Calcium, and Magnesium, with Some Remarks on the Solubility of Calcium Phospate in Serum and on the Pathogenesis of Tetany, J. Biol. Chem. **66**: 217, 1925.

48. Greenburg, D. M., and Mackey, M. A.: The Effect of Parathyroid Extract on the Blood Magnesium, J. Biol. Chem. **48**:765, 1932.

49. Bulger, H. A., and Gausmann, F.: Magnesium Metabolism in Hyperparathyroidism, J. Clin. Invest. **12**:1135, 1933.

50. Colby, R. W., and Frye, C. M.: Effects of Feeding Various Levels of Calcium, Potassium, and Magnesium to Rats, Am. J. Physiol. **166**: 209, 1951.

51. Colby, R. W., and Frye, C. M.: Effects of Feeding High Levels of Protein and Calcium in Rat Rations on the Magnesium Deficiency Syndrome, Am. J. Physiol. **166**:408, 1951.

52. Sjollema, D.: Nutritional and Metabolic Disorders in Cattle, Nutrition Abstr. & Rev. **1**:621, 1932.

53. Miller, J. F.: Tetany Due to Deficiency in Magnesium: Its Occurrence in a Child of 6 Years with Associated Osteochondrosis of Capital Epiphysis of Femur (Legg-Perthes Disease), Am. J. Dis. Child. **67**:117, 1944.

54. Dennis, W., and Talbot, F. B.: Calcium in the Blood of Children, Am. J. Dis. Child. **21**:29, 1921.

55. Gardner, L. I.; MacLachlan, E. A.; Pick, W.; Terry, M. L., and Butler, A. M.: Etiologic Factors in Tetany of Newly Born Infants, Pediatrics **5**:228, 1950.

56. Hirschfelder, A. D., and Haury, V. G.: Clinical Manifestations of High and Low Magnesium: Dangers of Epsom Salt Purgation in Nephritis, J. A. M. A. **102**:1138, 1934.

57. Walker, B. S., and Walker, E. O.: Normal Magnesium Metabolism and Its Significant Disturbances, J. Lab. & Clin. Med. **21**:713, 1936.

58. Creery, R. D. G., and Neill, D. W.: Idiopathic Hypercalcemia in Infants with Failure to Survive, Lancet **2**:110, 1954.

Muscular Dystrophy

I. History, Clinical Status, Muscle Strength, and Biopsy Findings

G. H. FETTERMAN, M.D.
M. J. WRATNEY, B.S., M.Ed.
J. S. DONALDSON, M.D.
and
T. S. DANOWSKI, M.D., Pittsburgh

The etiology of juvenile muscular dystrophy remains obscure despite many decades of clinical and laboratory observations.* The establishment of a program of preventive and remedial care for such patients in this hospital stimulated us to repeat and reassess some of the older observations and to report our findings. The clinical history, spinal fluid findings, motor status, and biopsy material from a group of children with juvenile muscular dystrophy are herein presented.

MATERIAL AND METHODS

Thirty-one children with a history of motor weakness suggestive of muscular dystrophy have been seen in the course of this series of studies. History of the familial incidence of the disease, if any, and of its onset was obtained and the patient's current status established. The strength of muscle groups was evaluated by the physiotherapist (M. J. W.) in accordance with motor function against gravity and against resistance. Biopsies of deltoid and of gastrocnemius muscles were then carried out under general anesthesia. Muscle strength was reevaluated at intervals following the operation.

RESULTS

A. The Patient Population.—An antecedent history of a debility characterized by muscular weakness was only rarely obtained in this group of 27 boys and 4 girls. The illness had been present on the maternal side in one instance and not at all on the paternal. Of the 31 children herein reported almost one-third had one or more siblings, alive or dead, who had progressive loss of muscular strength. These were usually boys. These findings, summarized in Table I, are in keeping with the reports of other workers but show a lower incidence of muscle disease in relatives other than siblings.†

The age of onset varied from 2 to 10 years. Developmental history related to crawling and walking often indicated retardation. At the time the patients were first seen the symptoms had been present for 6 months to 12 years. More than one-half of the patients were still ambulatory, while the remainder had been leading a wheel-chair or bed existence for one to eight years. These findings are summarized in Table II, together with other pertinent information concerning their physical status.

Results of spinal fluid examinations were all negative in those patients in whom it was possible to perform a lumbar puncture (Table III).

B. Muscular Strength.—The 31 patients in this group have been arranged in Table IV in the order of the averaged muscular strength, beginning with those least involved. The rating scale is indicated in the footnote to the Table. It should be noted first that, with one possible exception (D. H.), all of the muscle groups tested showed impairment. This appeared to be symmetrical and equal. In any particular patient the loss of motor strength was more pronounced in the lower extremities than in the upper; T. W.,

Submitted for publication Aug. 31, 1955.

Aided by grants from the Muscular Dystrophy Association of America, Incorporated.

From the Children's Hospital and the Departments of Pathology, Orthopedics, and Research Medicine of the University of Pittsburgh School of Medicine.

* References 1-7.

† References 8-17.

Table I

OCCURRENCE OF MUSCLE WEAKNESS IN FAMILIES OF CHILDREN WITH MUSCULAR DYSTROPHY

	MATERNAL						PATERNAL						SIBLINGS		
Patient Born	Mother	Grand-parents	Uncles	Aunts		COUSINS Male Female	Father	Grand-parents	Uncles	Aunts	COUSINS Male Female		Male	Female	
D.H. 9/23/45	0	00	00	0000		00000 0000	0	00	0		0		0+	0+00	
L.S. 3/23/39	0	00	0+0	00		0	0	00	00		00 00			0	
R.H. 8/8/43	0	00	00	0000		00000 0000	0	00	0		0		0+	0+00	
K.S. 7/3/38	0	00	000	0		00000 00000	0	00	000000	00000 0	0000 000000 0000 0		0+	00	
J.M. 1/3/44															
T.W. 5/15/45	Adopted														
D.E. 3/13/46	0	00	Half 00	0	Half 00000	00000 0000 00000 000	0	00		0			0+ Step 00	0	Step 000
W.S. 2/15/46	0	00	00	0		000	0	00	0	00	0000 0000			0000	
G.W. 1/11/47	0	00		0		0 0	0	00							
J.C. 4/7/47	0	00	0				0	00	0000	0000	0000 00000		0		
T.M. 3/8/43	0	00	0				0	00	00	0	0000 0 00				
R.S. 2/15/45	0	00	00	0		000	0	00	0	00	0000 0000		0+ Step 00	0	Step 000
L.B. 3/29/39	0	00	000000	000		0000 0000	0	00	00	00000	00000 00			0	
J.B. 3/13/43															
R.S. 7/3/38	0	00	00	00		00000 00000 0000 0000	0	00	00	00000	00000 0000 00		0		
C.P. 6/23/45	0	00	Half 000	00		0000 00000 00 00000	0	00	00000 0000	0	0000 00000 000 00000 0000		00 0+0+	00	
T.H. 4/27/45	0	00		00			0	00	0000	00	00000 00000		000	0	
P.Do. 3/21/47	0	00	00	00		0000 0000	0	00	0000	000	00 0			0	
C.H. 8/7/42	0	00	0000	000		0000 0000000	0	00	0000	00	0000 000000 000		0	Half 00	
G.Z. 11/17/44	0	00	000	0000		00000 0000	0	00	0	00	0 000			0	
W.H. 11/30/40	0	00	000	0		00000 00000	0	00	000000	00000 0	0000 000000 0000 000000 0		0+	00	
D.D. 4/24/37	0	00	00				0	00					0	0	
J.O. 10/15/31	0	00	00000	0000		00 0000 0000	0	00	000000	000	00000 000000		0	0	
R.T. 3/15/42	0	00		000		00 0	0	00	0					0	
G.P. 7/1/38	0	00	Half 000	00		000 0000000 000 0000	0	00	000000 000	0	0000 000000 0000 000000 00		00 0+0+	00	
J.R. 17/7/50	0	00	0	000		000	0	00	0		0		00		
R.J. 10/8/51	0	00		00		0 0	0	00		000	0		00		
D.M. 4/28/48	0	00	000	00		0000 000	0	00	Half 0	00	Half 0000	000000	0+000	000	
A.L. 3/10/43	0	00	0	00000		00000 0000 00000 000	0	00	000	000	000	00000			
C.B. 7/8/44	0	00	00000	00		0000 00000 00	0	00					00		
T.C. 7/24/38	0	00	0000 000	0000		0000	0	00	00	0	000	000000 000		0	

Table II

EARLY DEVELOPMENT, ONSET, AND PHYSICAL FINDINGS IN CHILDREN WITH MUSCULAR DYSTROPHY

PATIENT	DEVELOPMENT (Months -) Sat	Crawl	Walk	Teeth	Talk	AGE OF ONSET Yrs-Mos	INITIAL STATUS Walking	Short or Tight Musculature	CONTRACTURES
D.H.	6	9	12	6	20	7	yes	H.S.	Knee flex.-plantar flex.
L.S.	5 ½	7	12	13	18	2	yes	H.S.	Arms int.rot.-wrists ext.-legs int.rot.-plantar flex.
R.H.	6		14	8	24	10	yes	H.S.	Plantar flex.
K.S.	6	9	12	9+	18	5	yes	none	Left plantar flex.
J.M.							yes	none	Plantar flex.
T.W.	?	18	24	?	24	5 6	yes	H.S.	Plantar flex.
D.E.	5	8	?	10	36	6	no	H.S.	Elbows flex.-L & R pronation -knees flex.-hips flex.-Plantar flex.
W.S.	12	18	24	12	12	7	yes	H.S.	Plantar flex.-arms int. rot.
G.W.	6	11	16	7	14	7	yes	none	L & R pronation -knees flex.-Plantar flex.
J.C.	7	10	16	3 ½	18	2 6	yes	none	Plantar flex.
T.M.	6	9	12	9	24	7		H.S.	Plantar flex.-hips flex.-hips ext. legs ext. rot. arms pro.-L elbow ext. & flex.
R.S.	16	18	36	12	18	9	no	H.S.	Plantar flex.-L & R pronation
L.W.	7	18	14	9	11	5 6	no	H.S.-H.C.	Knee flex.-abduct.& hip flex.all L & R
J.B.								H.C.	
E.S.	12	15	16	8	18	12		H.S.	Plantar flex.-knee flex.-arm adduct.-pronation arm inward rotation -elbow flex.-all L & R -limited in shoulder flex.
C.P.	9	9	24	?	18	6		H.S.	Plantar flex. pronation
T.H.	15	8	18	?	?	6	no	none	Hip flex.-plantar flex.-pronation and arm int. rot.-all L & R
P.Do.	?	?	9	12	4		no	H.S.	Neck extension -pronation & internal rotation of both arms -hip flexion & plantar flexion -both legs
C.H.	6	8	18	3	18	9	no	H.S.	Hip flex.-knee flex.-plantar flex.
G.Z.	11	8	11	7	18	3 6	no	H.S.	Hip flex.-knee flex.-plantar flex.-elbow flex.-pronation -int.rot. of arms -all L & R
W.H.	slow	slow	slow	slow	slow			H.S.	All L & R -abduct. and ext.rot.of legs-Plantar flex.-hip flex.-pronation & int. rot. of arms
D.D.	?	9	18	6	18	2	no	H.S.	Supination of feet (both)
J.O.	6	8	15	9	15	7	no	H.S.	Plantar flex.-hip flex.-elbow flex. pronation & int.rot. of arms-all L & R
R.T.	?	?	?	5	6	5	no	H.S.	Left leg -external rotation -both legs -hip flexion
G.P.	6	9	16	?	18	6			Hip flex.-knee flex.-plantar flex.-elbow flex.-pronat.& -wrist flex.-int.rot.of arms -all L & R
J.R.	0	0	0	7	18	9	no	H.S.	Hip flex.-knee flex.-pronation -L & R
R.J.	4	7	10	7	12	1 4	no	No Data	No Data
D.M.	7	11	36	8	7	8	no		Elbow flex.-shoulder flex. & abduction hip flex.-knee flex.-plantar flex.-hip abduction H.S. - all L & R
A.L.								H.S.-H.C.	Hip flex.-knee flex.-L & R
C.B.	6	6	0	7 ½	good	4	no	H.S.	Hip flex.-knee flex.-plantar flex.L & R
E.G.	6	6	12	5	12	6			Arms limited in shoulder flexion -wrist, elbow & finger flexion contractures -R arm in pronation & internal rotation-L in ext. rot. Both legs in ext. rot. -hip, knee and plantar flexion

G. W., H. S., and E. S. are exceptions in that an equal or greater degree of upper limb involvement was present. The greater involvement of the lower limbs is most apparent in the more severely ill children. These findings are in keeping with other studies.‡

C. Results of Biopsy Examinations.—1. Collection and Preparation of Specimens: In 21 of 22 of the patients from this series, biopsy specimens were obtained from one deltoid and one gastrocnemius muscle. In one child, biopsy was done only on a gastrocnemius. These paired specimens were usually but not always from the same side.

Table III

SPINAL FLUID FINDINGS IN MUSCULAR DYSTROPHY

Patient	Cells/mm³	Kolmer	Coll. gold	Prot. (mg%)	Sugar (mg%)
L.E.	0	neg.	0000000000	40	
E.S.	0	neg.	0000000000	12	64
J.M.	0	neg.		13	72
T.W.	2 PMN	neg.	0000000000	13	64
W.S.	0	neg.	0000000000	12	62
J.C.	0	neg.	0000000000	15	70
T.W.	1 Lymph	neg.	0000000000	20	
H.S.	0	neg.	0000000000	17	62
L.W.	1 Lymph	neg.		36	70
E.S.	1 Lymph	neg.	0000000000	48	57
C.P.	0	neg.	0000000000	20	65
T.H.	0	neg.		25	66
P.De.	0	neg.	0000000000	15	55
C.B.	0	neg.		15	60
G.Z.	0	neg.		62	81
W.S.	0	neg.	0000000000	12	64
D.D.	0			22	72
J.G.	0	neg.		20	
G.P.	0	neg.		30	66
D.W.	2 Lymph 2 PMN	neg. neg.		80 20	100 50
A.L.	0	neg.	0000000000	13	72

The biopsy specimens were removed by sharp dissection in the operating room. Care was taken not to injure the innervation, and the insertion of the muscle was respected. Each specimen was divided, one portion being saved for chemical analysis and the other prepared for histologic examination. The segments for histologic examination were usually placed directly into a neutralized 10% formalin solution. In a few instances the specimens were spread out on cardboard and kept moist in saline for 15 minutes before immersion in the fixative. Following overnight fixation the specimens were embedded in paraffin and sections cut parallel to the long axis of the muscle fibers. When sufficient tissue was submitted, blocks were also cut in cross section. Sections were stained with hematoxylin and eosin.

The preparation of these muscle specimens did not include special staining of nerves, though we recognize that such methods of examination may contribute to the diagnostic value of muscle biopsies in the various muscular atrophies. Additional wet tissue was not available for frozen sections.

2. Gross Appearance: The gross appearance of the muscle biopsy specimens varied considerably. Some were indistinguishable from normal muscle, but many other specimens were pale, yellow, yellowish-tan, or yellowish-pink. The fatty character of several specimens was recognizable by the unaided eye.

3. Microscopic Appearance: Since the cases in this series were for the most part clinically typical of muscular dystrophy, there was little "pressure" placed upon the pathologist for definitive diagnosis. Nevertheless the muscle biopsy specimens from each case were studied by the pathologist without any knowledge of the clinical findings. In the examination of the muscle biopsies in these 22 patients the pathologist tried to evaluate the cases from the standpoint of characteristic changes, severity of the process, and the presence or absence of pseudo hypertrophy.

In 20 of the cases a histologic diagnosis of muscular dystrophy was returned. In one of the remaining two cases, considered as atypical from the standpoint of the histologic appearance of the skeletal muscle submitted, the pathologist was satisfied that his original opinion was in error. Although in each of these cases there were areas in the microscopic preparations where the grouping of atrophic muscle fibers imitated that appearance which is so common in neurogenic muscular atrophy, other areas presented alterations of individual fibers giving a histologic picture like that seen in muscular dystrophy. In most instances, however, histologic findings compatible with or char-

‡ References 12 and 18.

Table IV

FUNCTION OF MUSCLE GROUPS IN CHILDREN WITH MUSCULAR DYSTROPHY*

Patient	Age - Yr.	Sex - Mo.	Trunk R.	Trunk L.	Abdominals R.	Abdominals L.	Lower extremities R.	Lower extremities L.	Neck R.	Neck L.	Upper extremities R.	Upper extremities L.
D.H.	7	1,F	100	90	75	75	80	82	32	32	85	80
L.K.	13	8,M	25	25	75	75	71	74	50	50	80	78
R.H.	10	10,F	50	50	40	40	71	70	45	45	75	75
E.S.	5	7,M	75	75	33	35	64	64	35	35	78	71
J.M.	9	3,M	40	40	40	40	62	62	45	45	70	66
T.W.	7	8,M	65	63	40	40	71	71	25	25	73	74
D.E.	7	5,M	60	60	60	60	62	61	20	20	66	58
W.S.	7	10,M	60	60	40	40	61	56	40	40	63	64
G.W.	6	8,M	35	35	75	75	61	67	30	20	51	58
J.C.	5	6,M	60	60	35	35	49	48	45	45	61	59
T.M.	9	8,M	25	25	45	38	50	54	42	30	67	67
H.S.	8	13,M	50	50	35	35	47	46	35	35	48	48
L.W.	13	8,M	35	35	40	40	50	51	25	25	63	54
J.R.	10	11,M	40	40	40	40	38	42	30	30	48	48
E.S.	14	8,M	35	35	35	38	56	52	25	20	49	51
C.P.	7	6,M	40	40	35	35	46	44	25	25	49	49
T.H.	7	10,M	25	25	25	25	50	44	38	32	54	53
P.De.	5	11,M	25	25	40	40	42	42	15	15	51	53
C.K.	10	7,M	25	25	25	25	39	39	25	25	59	56
G.Z.	8	1,M			40	40	49	45	25	25	62	55
W.S.	13	4,M	35	35	30	30	30	32	30	30	45	44
D.D.	15	7,M	25	25	35	35	33	28	38	40	26	25
J.O.	11	1,M	15	15	35	35	36	40	25	25	50	47
R.B.	10	7,M	25	25	25	25	32	32	25	25	48	50
G.P.	14	8,M	25	15	25	15	26	26	25	25	45	44
J.B.	2	5,M	3	8	30	30	32	33	30	30	34	37
B.J.	2	6,M	10	10	15	15	18	18	50	50	30	39
D.W.	12	10,M	10	10	25	25	26	26	25	15	41	42
A.L.	7	9,F	0	0	12	18	32	35	20	25	37	39
C.B.	8	6,F			15	15	25	26	15	15		
E.G.	15	4,M			20	20	3	3	2	2	6	1

* Graded in accordance with the following table: intermediate grades, i.e., P+ or P- represents an estimated 10 per cent less or greater function
N or 100% = NORMAL = Function against gravity and normal resistance
G or 75% = GOOD = Function against gravity and some resistance
F or 50% = FAIR = Function against gravity only
P or 25% = POOR = Function in horizontal plane
T or 10% = TRACE = A few fibers have active function
N.P. or 0 = NO POWER

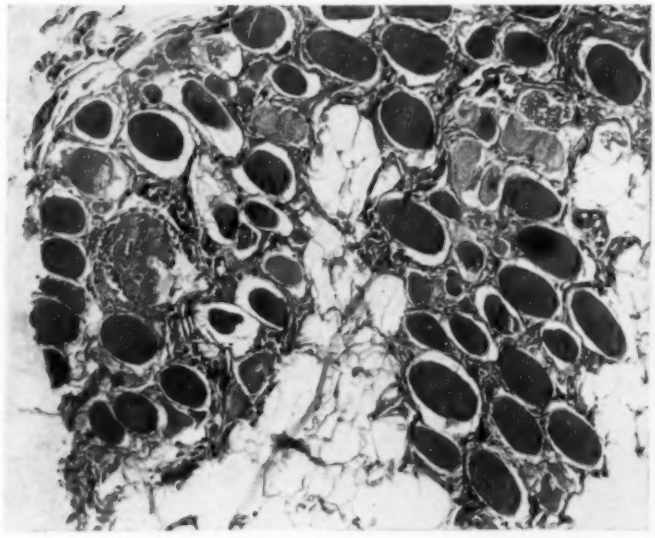


Fig. 1.—Patient W. S. A number of swollen muscle fibers and considerable fatty infiltration are seen. A degenerated muscle fiber at left presents erosion and phagocytosis; reduced approximately ⅓ from mag. × 140.

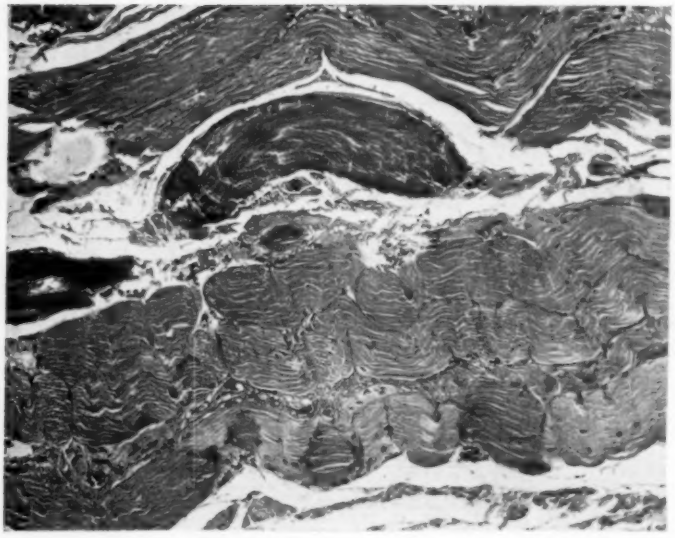


Fig. 2.—Patient L. W. A large swollen degenerating fiber may be seen in lower portion of upper half of picture; reduced approximately ⅙ from mag. × 140.

acteristic of muscular dystrophy were observed (Figs. 1-9).

4. Pattern of Involvement: The most helpful and characteristic histologic finding was in the pattern of involvement, that is, the presence of swollen, degenerated, or atrophic individual muscle fibers, lying intermingled with normal fibers or, at least, with fibers of dissimilar appearance.

This pattern should be well known, as it has been emphasized by a number of writers.§ It is best appreciated in contrast with the orderly pattern of neuropathic myopathies, such as amyotonia congenita, in which miniature or embryonic fibers are seen grouped in motor units, involving fascicles or portions

§ References 6, 7, and 19-22.

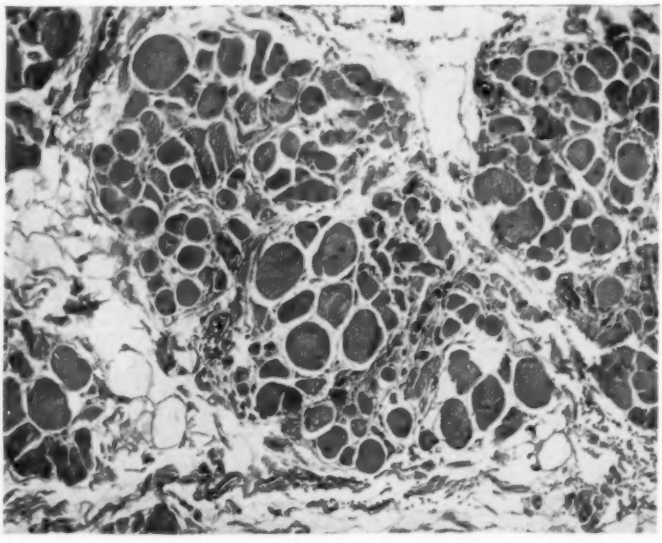


Fig. 3.—Patient D. M. Variation in size of individual fibers is illustrated. Splitting of muscle fibers and fatty infiltration are also seen; reduced approximately ⅙ from mag. × 140.

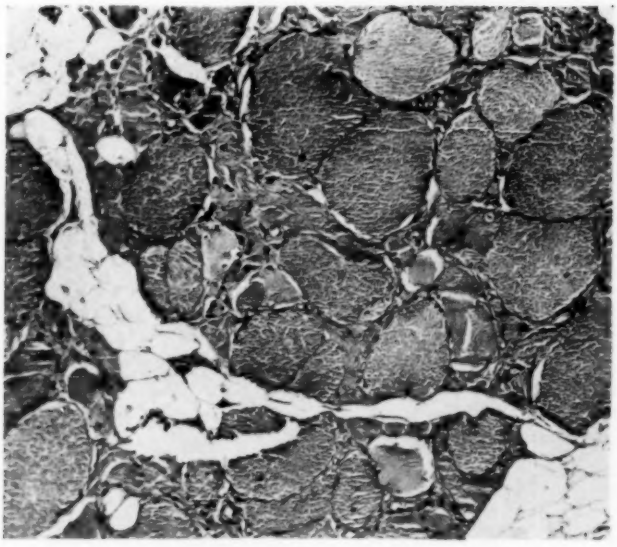


Fig. 4.—Patient E. S. Marked variation in size of muscle fibers, scarring, and fatty infiltration are shown; reduced approximately ⅕ from mag. × 140.

of fascicles, intermingled with fascicles or portions of fascicles consisting entirely of normal or hypertrophic fibers.

5. Appearance of Affected Muscle Fibers: The muscle fibers which displayed evidence of alteration varied considerably in their appearance. Some were swollen, with or without hyalinization. Many of these stained darkly. Longitudinal and cross striations were blurred or absent in many instances. Many fibers were vacuolated. A few large ones presented splitting with formation of smaller fibers. Late stages in the degeneration were erosion and phagocytosis. The phagocytic cells were usually macrophages, but in a few instances a sprinkling of neutrophilic leucocytes was observed among the cells surrounding dark-stainng, degenerated, and

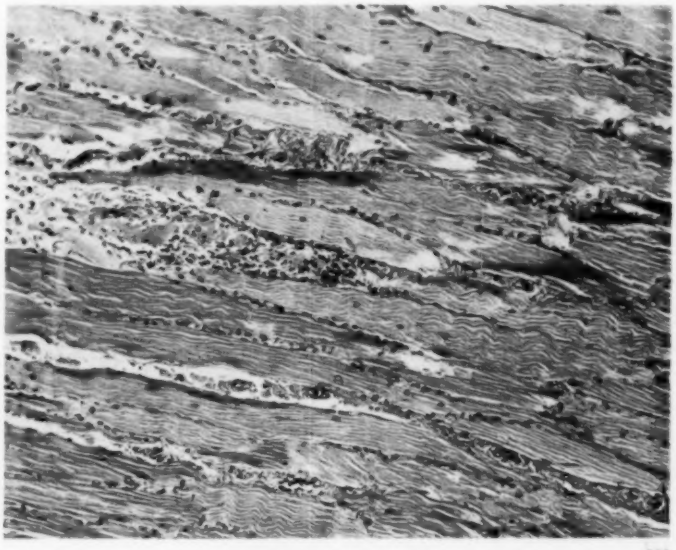


Fig. 5.—Patient C. P. A degenerated fiber undergoing erosion and phagocytosis is present at middle left; reduced approximately ⅙ from mag. × 140.

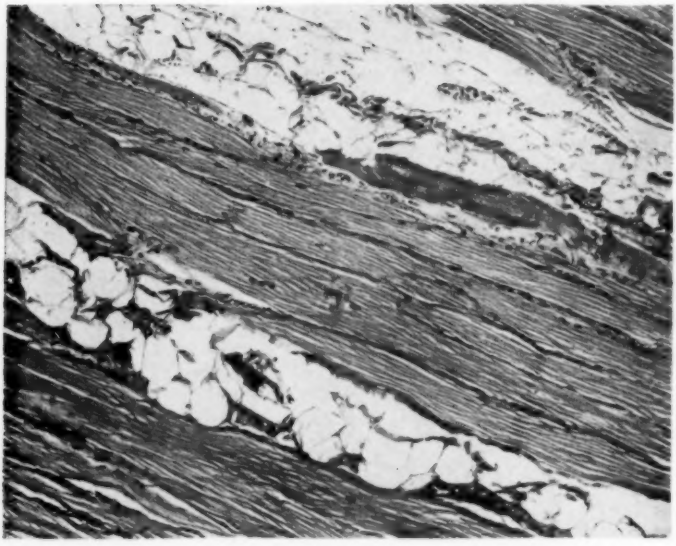


Fig. 6.—Patient W. S. Fatty infiltration is striking. At lower right border of upper fatty layer is a degenerated muscle fiber; reduced approximately ⅓ from mag. × 140.

partially eroded fibers. Many atrophic fibers were seen which retained cross striations; these, too, were usually scattered haphazardly throughout affected muscle. The presence of rows of sarcolemmal nuclei within the central portions of muscle fibers was rare in this material. In many of the specimens, however, longitudinal rows or clumps of conspicuous sarcolemmal nuclei were associated with extremely atrophic fibers. Sometimes the chains or clumps of darkly staining sarcolemmal nuclei were the only residua of damaged muscle fibers.

6. The Interstitial Connective Tissue: In many instances, there was considerable fibrosis. Fibroblasts in various stages of development were noted. The fibrous tissue in some areas contained sarcolemmal nuclei. More

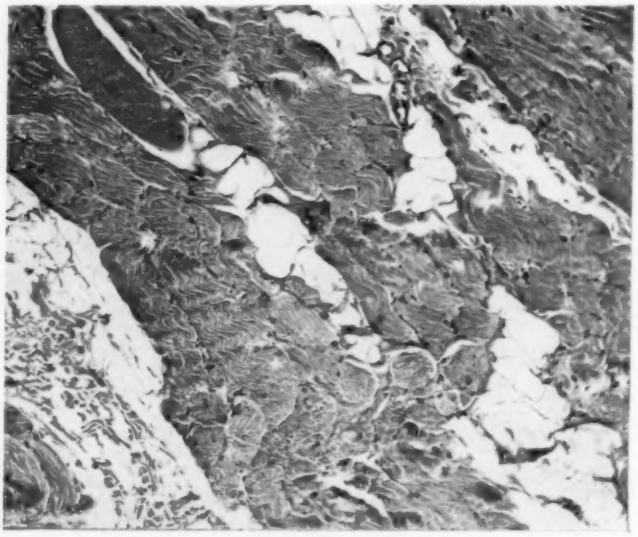


Fig. 7.—Patient H. S. There is fatty infiltration and some fibrosis. A single degenerated fiber is present at upper left; reduced approximately ⅓ from mag. × 140.

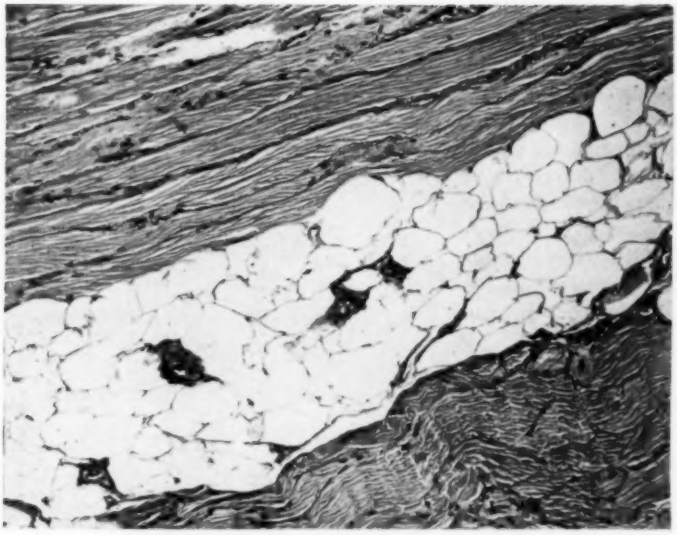


Fig. 8.—Patient D. D. This section presents fatty infiltration. The remaining muscle bundles are not remarkable; reduced approximately ⅙ from mag. × 140.

striking and more frequent was fatty infiltration. In those cases showing most fatty replacement there were usually fewer actively degenerating fibers observed.

Primary inflammation was not observed. Occasional small perivascular collections of lymphocytes were seen. The rare neutrophilic leucocytes were adjacent to severely degenerated fibers undergoing erosion and phagocytosis.

7. Intramuscular Nerves: Nerve changes were not demonstrable in our material. Muscle spindles appeared normal.

8. Artefacts: In the study of this biopsy material, as well as certain other muscle sections available which might be considered as controls, we noted certain individual muscle fibers with a dark "glassy" appearance. These were present in many cases; they were usually located at or very near the

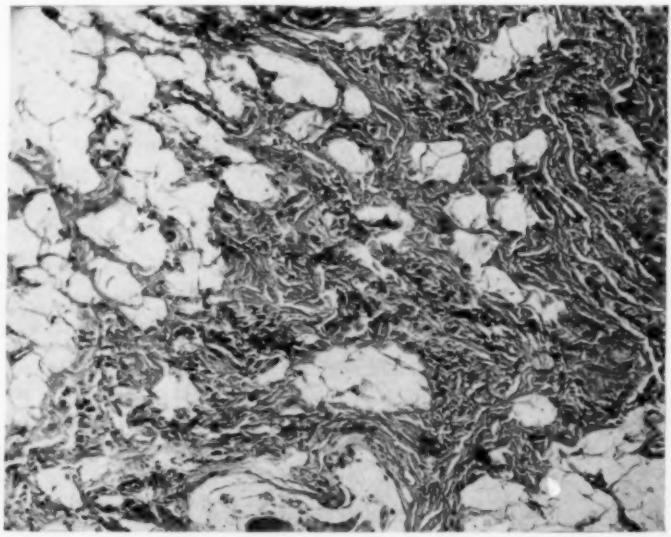


Fig. 9.—Patient R. B. Here may be seen an unusual degree of fibrosis. Many dark-staining residual sarcolemmal nuclei remain. There is also fatty infiltration; reduced approximately ⅙ from mag. × 140.

edges of the blocks. Present in normal as well as diseased muscle, they were thought to reflect changes induced by the slight trauma incidental to surgery or by the method of fixation employed. Such artefacts might upon occasion be troublesome to the pathologist, but were easily differentiated from truly degenerated fibers showing definite swelling, phagocytosis, and erosion in varying degree. An excellent discussion of artefacts in muscle sections is contained in the material presented by Adams, Denny-Brown, and Pearson.[7]

It is noteworthy that in a few cases the finding of partially eroded fibers representative of genuine change served to bolster a histologic diagnosis of muscular dystrophy. This was true in several specimens from muscles which displayed only early change.

9. Variations in Alterations Displayed by Individual Patients: It was interesting but not unexpected that there was often great variation in appearance between specimens from two muscles of the same patient. Further, in many instances there was marked variation among slides cut at various levels of the same blocks. This variation in most instances concerned the amount of fatty infiltration. However, the severity of muscle involvement was usually consistent in the various samplings.

10. Atypical Findings: In two patients (A. L. and J. C.), histopathologic diagnoses of "neuropathic muscular atrophy" were made by one of us (G. H. F.). In one of them (A. L.) a repeat biopsy over two years later was reported by one of us (G. H. F.) as "muscular dystrophy." Review of the original series of sections made us feel that the original diagnosis had perhaps been erroneous, but not certainly so. The case is atypical in more than one respect.

In the other case with atypical findings (J. C.), when our original diagnosis was questioned, the slides were submitted to a referee (Dr. Webb Haymaker, of the Armed Forces Institute of Pathology), who stated that the changes were representative of muscular dystrophy. We now believe his opinion to be correct. Histologic preparations from the biopsies in each of these two cases displayed in some areas grouping of altered fibers which was not unlike that seen in the neuropathic muscular atrophies. Such cases will always be troublesome according to present criteria.

11. Attempts to Quantitate Histologic Findings with Clinical Status: An attempt was made to evaluate the intensity of the lesion in accordance with two scales, with "definite" referring to changes thought to

Table V

RELATION OF MOTOR STRENGTH TO SEVERITY OF PATHOLOGICAL CHANGE IN MUSCLE BIOPSIES

Patient	Motor Strength of Biopsied Extremity (% of normal)	Motor Strength of Biopsied Muscles (% of normal)	Biopsy Findings
L.E.	L. Upper 78	L. Delt. Ant. 50 L. Delt. Post. 50	definite
	L. Lower 74	L. Gastroc. 100	definite
E.S.	L. Upper 71	L. Delt. Ant. 65 L. Delt. Post. 60	definite
	L. Lower 64	L. Gastroc. 75	def.-far-adv.
J.M.	L. Upper 66	L. Delt. Ant. 60 L. Delt. Post. 50	definite
	L. Lower 62	L. Gastroc. 90	definite
T.W.	L. Upper 74	L. Delt. Ant. 30 L. Delt. Post. 50	far-adv
	L. Lower 71	L. Gastroc. 70	definite
R.S.	L. Upper 64	L. Delt. Ant. 50 L. Delt. Post. 50	far-adv
	L. Lower 56	L. Gastroc. 65	definite
J.C.	L. Upper 50	L. Delt. Ant. 60 L. Delt. Post. 60	
	L. Lower 48	L. Gastroc. 75	far-adv.
T.M.	L. Upper 67	L. Delt. Ant. 60 L. Delt. Post. 60	definite
	L. Lower 54	L. Gastroc. 65	definite
H.S.	L. Upper 48	L. Delt. Ant. 50 L. Delt. Post. 50	definite
	L. Lower 46	L. Gastroc. -	far-adv.
L.H.	L. Upper 54	L. Delt. Ant. 25 L. Delt. Post. 25	far-adv.
	L. Lower 51	L. Gastroc. 75	far-adv.
K.S.	L. Upper 51	L. Delt. Ant. 40 L. Delt. Post 40	far-adv
	L. Lower 53	L. Gastroc. 50	far-adv.
C.P.	L. Upper 44	L. Delt. Ant. 50 L. Delt. Post. 50	definite
	L. Lower 40	L. Gastroc. -	definite
T.H.	L. Upper 53	L. Delt. Ant. 60 L. Delt. Post 50	definite
	L. Lower 44	L. Gastroc. 60	definite
P.D	L. Upper 53	L. Delt. Ant. 50 L. Delt. Post 50	def.-far-adv.
	L. Lower 42	L. Gastroc. 25	definite
C.K	L. Upper 56	L. Delt. Ant. 50 L. Delt. Post 50	definite
	L. Lower 30	L. Gastroc. 60	far-adv
G.Z.	L. Upper 55	L. Delt. Ant. - L. Delt. Post -	far-adv.
	L. Lower 45	L. Gastroc. -	far-adv.
R.S.	L. Upper 44	L. Delt. Ant. 25 L. Delt. Post 15	far-adv.
	L. Lower 32	L. Gastroc. 25	far-adv.
D.D.	L. Upper 35	L. Delt. Ant. 15 L. Delt. Post 10	far-adv.
	L. Lower 28	L. Gastroc. 25	far-adv
J.O.	L. Upper 67	L. Delt. Ant. 50 L. Delt. Post 50	far-adv
	L. Lower 40	L. Gastroc. 25	far-adv
R.B.	L. Upper 50	L. Delt. Ant. 25 L. Delt. Post 25	far-adv.
	L. Lower 32	L. Gastroc. 50	definite
G.P	L. Upper 44	L. Delt. Ant. 10 L. Delt. Post 10	far-adv
	L. Lower 36	L. Gastroc. 25	far-adv
D.H.	L. Upper 42	L. Delt. Ant 25 L. Delt. Post 25	
	L. Lower 25	L. Gastroc 15	far-adv
A.L.	L. Upper 36	L. Delt. Ant 40 L. Delt. Post 10	See text
	L. Lower 35	L. Gastroc 60	

Table VI

STRENGTH OF INDIVIDUAL MUSCLES PRIOR TO AND FOLLOWING BIOPSY

Pt.	Muscle	Before Biopsy (% of Normal)		AFTER BIOPSY															
				% of Normal		Mos. P oper.	% of Normal		Mos. P oper.	% of Normal		Mos. P oper.	% of Normal		Mos. P oper.	% of Normal		Mos. P oper.	% of Normal		Mos. P oper.
		R.	L.	R.	L.		R.	L.		R.	L.		R.	L.		R.	L.		R.	L.	
L.K.	Gastroc.	100	100	100	100	(10)	100	100	(21)												
	Delt.Ant.	80	50	60	60		50	80													
	Delt.Post.	60	50	60	60		60	60													
E.S.	Gastroc.	75	75	100	100	(13)	100	100	(15)	100	100	(20)									
	Delt.Ant.	65	65	60	60		60	60		65	65										
	Delt.Post.	65	65	50	50		60	60		60	60										
J.H.	Gastroc.	90	90	100	100	(6)	90	85	(12)	90	80	(13)									
	Delt.Ant.	60	60	60	60		60	60		60	60										
	Delt.Post.	50	50	50	60		50	50		40	50										
T.W.	Gastroc.	75	75	75	75	(9)	-	-	(16)	100	100	(19)									
	Delt.Ant.	50	50	50	50		50	50		50	50										
	Delt.Post.	50	50	50	50		50	50		40	40										
W.S.	Gastroc.	60	65	60	75	(8)	-	-	(12)	80	75	(16)									
	Delt.Ant.	50	50	50	50		50	50		50	50										
	Delt.Post.	50	50	50	50		60	50		40	50										
J.C.	Gastroc.	75	75	85	60	(8)	60	60	(11)	WMS		(13)	60	60	(24)	75	75	(17)	85	65	(22)
	Delt.Ant.	60	60	65	65		65	65		60	75		60	65		65	65		65	65	
	Delt.Post.	60	60	50	50		90	50		60	65		60	60		60	60		60	40	
T.M.	Gastroc.	65	65	75	75	(5)															
	Delt.Ant.	60	60	60	60																
	Delt.Post.	60	60	25	25																
H.S.	Gastroc.	-	-	50	50	(6)	-	-	(12)	-	-	(10)									
	Delt.Ant.	50	50	50	50		50	50		50	50										
	Delt.Post.	50	50	50	50		40	40		40	50										
L.B.	Gastroc.	75	75																		
	Delt.Ant.	15	25																		
	Delt.Post.	15	25																		
K.S.	Gastroc.	75	50																		
	Delt.Ant.	40	40																		
	Delt.Post.	40	40																		
C.P.	Gastroc.	-	-	85	85	(21)															
	Delt.Ant.	50	50	50	50																
	Delt.Post.	50	50	40	35																
T.H.	Gastroc.	80	80	25	25	(8)	50	50	(11)	25	25	(18)									
	Delt.Ant.	60	60	50	40		50	50		25	25										
	Delt.Post.	60	60	50	40		15	15		15	15										
P.D.	Gastroc.	35	35	-	-	(7)	40	60	(9)	60	60	(10)									
	Delt.Ant.	50	50	50	50		50	50		50	40										
	Delt.Post.	50	50	50	50		50	50		40	40										
C.K.	Gastroc.	40	40	50	50	(8)	50	60	(12)												
	Delt.Ant.	50	50	50	40		35	40													
	Delt.Post.	50	50	50	50		-	-													
G.Z.	Gastroc.	-	-	25	50	(11)	60	60	(19)	50	65	(16)									
	Delt.Ant.	-	-	10	25		10	25		15	15										
	Delt.Post.	-	-	10	10		10	15		15	10										
W.S.	Gastroc.	35	35	25	35	(15)	35	40	(18)	35	35	(21)									
	Delt.Ant.	25	25	25	25		25	35		35	40										
	Delt.Post.	15	15	10	15		25	35		10	10										
D.D.	Gastroc.	25	25																		
	Delt.Ant.	15	15																		
	Delt.Post.	10	10																		
J.O.	Gastroc.	35	35	60	50	(6)	60	50	(13)	65	65	(22)									
	Delt.Ant.	50	50	50	50		30	35		25	25										
	Delt.Post.	50	50	25	25		10	15		10	15										
E.B.	Gastroc.	50	50	50	50	(19)															
	Delt.Ant.	35	25	25	25																
	Delt.Post.	35	25	25	25																
A.P.	Gastroc.	35	35	15	15	(21)															
	Delt.Ant.	10	10	15	15																
	Delt.Post.	10	10	15	10																
D.W.	Gastroc.	15	15	15	15	(10)															
	Delt.Ant.	25	25	15	15																
	Delt.Post.	25	25	-	-																
A.L.	Gastroc.	50	40	25	25	(20)															
	Delt.Ant.	35	40	35	25																
	Delt.Post.	15	10	25	25																

be compatible with or perhaps even diagnostic of muscular dystrophy and "far-advanced" serving to identify those cases which had the most pronounced changes. The histologic criteria we used in grading the "severity" of the process were based upon the degree of muscle fiber loss or atrophy, fibrosis, and fatty infiltration. This gradation was made without prior knowledge of the clinical status of the patient and then compared with the muscle strength of limbs from which the material for biopsy was obtained. The findings are shown in Table V. It is immediately evident that a high positive correlation is present between the biopsy findings and the clinical status in the patients with muscle strength reduced below 50% of normal. On the other hand the presence of far-advanced histologic changes in the group with muscle strength still above 50% indicates that the histologic change precedes clinical deterioration.

D. Motor Strength Following Biopsy.—There is no evidence that the biopsy procedure by itself produced any harmful effect upon the muscle strength of the operated-on limb. It is apparent from Tables VI and VII that in the months following biopsy motor strength was about the same in the muscle groups and extremities which were operated on and those which were not, respectively.

Table VII

RELATIVE STRENGTH OF OPERATED AND NON-OPERATED EXTREMITIES FOLLOWING MUSCLE BIOPSY

Pt.	Extremity	Before Biopsy (% of Normal)		AFTER BIOPSY													
				% of Normal	Mos. p oper.	% of Normal	Mos. p oper.	% of Normal	Mos. p oper.	% of Normal	Mos. p oper.	% of Normal	Mos. p oper.	% of Normal	Mos. p oper.	% of Normal	Mos. p oper.
		R.	L.	R.	L.		R.	L.		R.	L.		R.	L.		R.	L.		R.	L.	
L.R.	Upper	80	78*	77	81	(10)	85	88	(21)												
	Lower	71	74*	73	73		86	86													
E.S.	Upper	70	71*	64	66	(13)	71	69	(15)	68	68	(21)									
	Lower	64	64*	59	66		69	61		62	62										
J.W.	Upper	70	66*	70	60	(6)	69	70	(12)	67	67	(15)									
	Lower	62	62*	52	54		61	59		55	57										
T.W.	Upper	73	74*	62	61	(9)	56	58	(15)	52	54	(19)									
	Lower	71	71*	68	66		51	53		53	54										
W.S.	Upper	63	64*	58	59	(8)	66	68	(12)	67	67	(16)									
	Lower	61	56*	56	53		68	68		52	50										
J.C.	Upper	61	50*	66	65	(8)	69	66	(11)	70	73	(15)	72	70	(14)	72	72	(17)	66	67	(22)
	Lower	49	48*	51	51		61	62		52	53		48	49		50	51		51	50	
T.W.	Upper	67	67*	53	52	(3)	65	65	(3)												
	Lower	55	56*	50	47		57	55													
H.S.	Upper	48	48*	49	48	(8)	46	47	(12)	53	53	(16)									
	Lower	47	49*	46	46		45	45		52	50										
L.R.	Upper	63	56*																		
	Lower	50	51*																		
E.S.	Upper	49	51*																		
	Lower	56	53*																		
C.P.	Upper	49	49*	80	49	(20)															
	Lower	46	44*	52	50																
T.H.	Upper	54	53*	44	42	(8)	45	45	(11)	37	36	(18)									
	Lower	50	44*	33	40		43	43		28	28										
P.D.	Upper	51	53*	57	60	(7)	60	58	(9)	61	62	(10)									
	Lower	42	42*	45	46		50	48		50	53										
C.K.	Upper	59	56*	52	54	(8)	62	62	(12)												
	Lower	39	39*	40	42		60	56													
G.Z.	Upper	62	55*	50	46	(11)	47	43	(13)	44	44	(16)									
	Lower	49	45*	35	32		38	36		41	37										
W.S.	Upper	45	46*	42	40	(12)	43	41	(15)	41	42	(21)									
	Lower	30	32*	21	22		27	25		28	29										
D.D.	Upper	36	35*																		
	Lower	33	28*																		
J.O.	Upper	50	47*	44	42	(8)	40	39	(12)	43	41	(22)									
	Lower	36	40*	36	40		35	36		39	40										
R.B.	Upper	48	50*	47	46	(19)															
	Lower	32	32*	33	33																
A.P.	Upper	45	44*	37	29	(20)															
	Lower	35	26*	17	14																
D.M.	Upper	41	42	34	37	(19)															
	Lower	26	25*	25	26																
A.L.	Upper	37	38	42	40	(28)															
	Lower	32	35	36	34																

* Indicates extremity operated

COMMENT

These measurements of muscle strength and studies of muscle biopsy specimens obtained in a group of children with histories and findings suggestive of muscular dystrophy permit certain useful generalizations.

First, in all of these children with a muscular debility which had appeared and run to date a course thought to be compatible with muscular dystrophy careful testing of muscle groups almost always revealed universal or virtually universal impairment. This was true even though weakness in those groups had not been grossly apparent clinically. Normal function against gravity and resistance were only rarely encountered and then only in the muscle groups of the hands and the feet. Second, insofar as could be determined, the involvement appeared to be equal in degree on both sides. Third, the defect proved to be constant in repeated or serial examinations, provided that care was taken to duplicate the test conditions. This last point is discussed in greater detail in the serial examinations conducted in an evaluation of a protein hydrolysate regimen in these patients.[28]

Several writers have expressed their belief in the value of biopsy in muscular dystrophy, while acknowledging its limitations.|| The muscle changes which we and others consider as most characteristic of muscular dystrophy have been mentioned. Most important among these changes is the tendency for scattered individual muscle fibers to be involved. Diseased fibers are recognizable by changes in size, staining qualities, conspicuous sarcolemmal nuclei, splitting of large fibers, blurring of striations, vacuolization, and, in the final stage, phagocytosis and erosion were present in at least 7 of the 22 cases from which biopsy specimens were examined. Interstitial changes included fatty infiltration and/or fibrosis.

We believe the muscle biopsy to be of considerable value as an aid in the clinical diagnosis of muscular dystrophy, but only

|| References 7 and 20-22.

if the histologic appearance is quite characteristic. In the two cases of our series where it seemed inconclusive, it may be that some difference in quality of the disease existed. Another explanation might be that both neuropathic and myopathic disorders coexisted in each of these two patients. It should be remembered, however, that, as in any application of the biopsy method, the value depends to a great extent upon the choice of tissue. In muscular or neuromuscular disorders, the sampling cannot be as precise or as extensive as one would like it. When one realizes the differences which may exist in various levels of the same small block of tissue, it is surprising how often a consistent histologic picture is present.

With respect to the muscle biopsies, a further point to be made is that the changes are roughly quantitative as well as qualitative. The pathologist had no knowledge of the status of the individual patient in evaluating the biopsy. Yet, the general features of the specimen, such as the amount of fat in relation to the amount of muscle and the specific changes in the muscle, permitted an accurate quantitative prediction of the degree of clinical involvement. Thus, all of the patients with marked clinical debility also had far-advanced histologic changes. On the other hand, these histologic alterations seem to precede the clinical changes, since in a number of the patients in the less-involved group muscle strength was relatively well maintained even though the biopsy showed far-advanced disease. Finally, it should be pointed out that in terms of the subsequent course of the illness biopsy had no evident deleterious effect on muscle strength. Months or years later the extremities and muscles which were operated on and those which were not were still comparable in strength.

These findings with regard to muscle strength and biopsy findings are not surprising and of course present no fundamentally new facts. They do serve, however, to inject a quantitative aspect into a mysterious disease. However, it is obvious that in these studies we have only characterized the patient who has an entity which looks like and probably is muscular dystrophy. We have presented no control material which would serve to differentiate muscular dystrophy from other muscular, neuromuscular, or neurologic disorders.

SUMMARY AND CONCLUSIONS

Study of a group of children with a history compatible with muscular dystrophy has shown (1) that losses of muscle strength, as revealed by careful testing of muscle groups, are symmetrical and virtually universal; (2) that the histologic lesion is always far advanced in the patients with the most pronounced muscle debilities but that such changes may precede the loss in muscle strength; (3) that biopsy does not cause further deterioration of muscle strength in the operated-on extremity.

REFERENCES

1. Proceedings of the First and Second Medical Conferences of the Muscular Dystrophy Association of America, Inc., held in New York, April 14-15, 1951 and May 17-18, 1952, edited by A. T. Milhorat, New York, Muscular Dystrophy Association of America, Inc., 1953.

2. Nevin, S.: Primary Diseases of Voluntary Muscles, J. Neurol. & Psychiat. **1**:120-141 (April) 1938.

3. Tyler, F. H., and Wintrobe, N. M.: Studies in Disorders of Muscle: I. Problem of Progressive Muscular Dystrophy, Ann. Int. Med. **32**:72-79 (Jan.) 1950.

4. Viets, H. R., and Brown, M. R.: Medical Progress: Diseases of Muscles, New England J. Med. **245**:647-653 (Oct. 25) 1951.

5. Tyler, F. H., and Perkoff, G. T.: Studies in Disorders of Muscle: VI. Is Progressive Muscular Dystrophy an Endocrine or Metabolic Disorder? A. M. A. Arch. Int. Med. **88**:175-190 (Aug.) 1951.

6. Bing, R., and Haymaker, W.: Textbook of Nervous Diseases, Ed. 5, St. Louis, C. V. Mosby Company, 1939.

7. Adams, R. D.; Denny-Brown, D., and Pearson, C. M.: Diseases of Muscle: A Study in Pathology, New York, Paul B. Hoeber, Inc., 1953.

8. Hough, G. D., Jr.: Hereditary Aspects of Progressive Pseudohypertrophic Muscular Dystrophy, New England J. Med. **214**:1189-1191 (June 11) 1936.

9. Milhorat, A. T., and Wolff, H. G.: Studies in Diseases of Muscle: Heredity of Progressive Muscular Dystrophy; Relationship Between Age at Onset of Symptoms and Clinical Course, Arch. Neurol & Psychiat. **49**:641-654 (May) 1943.

10. Bell, J.: On Pseudohypertrophic and Allied Types of Progressive Muscular Dystrophy, in Nervous Disease and Muscular Dystrophies in the Treasury of Human Inheritance, edited by R. A. Fisher, London, Cambridge University Press, 1943, Vol. 4, Pt. 4.

11. Tyler, F. H., and Stephens, F. E.: Studies in Disorders of Muscle: Clinical Manifestations and Inheritance of Facioscapulohumeral Dystrophy in Large Family, Ann. Int. Med. **32**:640-660 (April) 1950.

12. Tyler, F. H., and Stephens, F. E.: Studies in Disorders of Muscle: IV. The Clinical Manifestations and Inheritance of Childhood Progressive Muscular Dystrophy, Ann. Int. Med. **35**:169-185 (July) 1951; Correction **35**:1164 (Nov.) 1951.

13. Brown, M. R.: Incidence and Heredity of Muscular Dystrophy: Study of 71 Patients Admitted to Massachusetts General Hospital, New England J. Med. **244**:88-90 (Jan. 18) 1951.

14. Becker, P. E.: Eine klinisch-genetische Untersuchung der Dystrophia musculorum progressiva (Erb), Arch. Psychiat. **189**:1-22, 1952.

15. Stephens, F. E.: Inheritance of Diseases Primary in Muscles, Am. J. Med. **15**:558-569 (Oct.) 1953.

16. Levison, H.: Dystrophia Musculorum Progressiva: Clinical and Diagnostic Criteria; Inheritance, Acta psychiat. et neurol. scandinav., Supp. 76, pp. 1-176, 1951.

17. Fraser, F. C.: Medical Genetics in Pediatrics, J. Pediat. **44**:85-103 (Jan.) 1954.

18. Tyler, F. H.: Studies in Disorders of Muscle: "Pseudohypertrophy" of Muscle in Progressive Muscular Dystrophy and Other Neuromuscular Diseases, Arch. Neurol. & Psychiat. **63**:425-432 (March) 1950.

19. Hassin, G. B.: Histopathology of Progressive Muscular Dystrophy, J. Neuropath. & Exper. Neurol. **2**:315-325 (Oct.) 1943.

20. Bowden, R. E. M., and Gutmann, E.: Clinical Value of Muscle Biopsies, Lancet **2**:768-771 (Dec. 15) 1945.

21. Ramsey, R. H., and McCarroll, H. R.: Problem of Muscular Dystrophies, J. A. M. A. **150**:659-662 (Oct. 18) 1952.

22. Rosenberg, H. S., and McAdams, A. J.: Infantile Progressive Muscular Atrophy: Value of Muscle Biopsy in the Diagnosis of and Its Differentiation from Muscular Dystrophy, A. M. A. Arch. Path. **58**:604-612 (Dec.) 1954.

23. Donaldson, J. S.; Wratney, M. J.; Pascassio, A.; Weigand, F. A., and Danowski, T. S.: Muscular Dystrophy: VIII. Trials of Protein Hydrolysate, Vitamin Supplements, and Physiotherapy, A. M. A. J. Dis. Child., to be published.

Muscular Dystrophy

II. Radiologic Findings in Relation to Severity of Disease

B. GIRDANY, M.D.
and
T. S. DANOWSKI, M.D., Pittsburgh

Changes demonstrable by x-rays occur in the long bones, spine, and soft tissues of patients with muscular dystrophy.* Most authors have regarded these findings as part of the disease; they have not correlated them with the severity of the disease. Lewitan and Nathanson [15] pointed out that, "the bone changes are purely secondary to the muscle involvement."

The hospitalization of a group of children with muscular dystrophy has provided the opportunity for a study correlating the radiographic changes with the severity of the disease.

MATERIAL AND METHODS

Roentgenograms of the vertebral column, skull, long bones, wrists, and thorax were made of 31 children whose history, physical findings, laboratory studies, and muscle biopsy were compatible with the diagnosis of juvenile form of muscular dystrophy. Films of the spine were examined for signs of scoliosis, lordosis, kyphosis, and "caninization" (i. e., apparent increase in the altitude of the vertebral bodies) and films of the long bones and pelvis for coxa valga, demineralization, and overtubulation. The soft-tissue masses of the extremities and the presence of striations indicative of fatty infiltration within the muscles were noted. Bone age was estimated from films of the left hand according to the methods and standards of Greulich and Pyle.[16] Cardiothoracic ratios were measured from teleoroentgenograms of those subjects who were ambulatory.

The radiologist had no direct knowledge concerning the duration of the disease or the physical status of the individual patients. He attempted to quantitate the degree of change on the scale of 0 to 3+; 0 indicated no change, and 3+ indicated the most marked changes. These findings were then compared with the severity of the disease as determined by examinations of the motor power of muscle groups against gravity and against resistance in accordance with the scale presented in other reports from this laboratory.†

RESULTS

Table I summarizes the radiographic findings in this group of children with muscular dystrophy. The patients are listed in the order of decreasing muscle strength.

I. Spine.—Scoliosis occurred oftener and to a greater degree in patients with more extensive muscular involvement. Lordosis was present in children with early and late phases of disease as a compensatory phenomenon in the maintenance of the upright position; kyphosis was only occasionally present.

Lateral roentgenograms of the spine in some instances showed an apparent increase in the altitude of the lumbar vertebral bodies. The height-width relationships resembled those seen in quadrupeds, hence the term "caninization." This nonspecific change is seen in children chronically bedridden for any cause whatsoever. Since it is not as obvious in the anteroposterior roentgenograms, it is possible that the increase in the height of the individual vertebral bodies is more apparent than real and is due to a decreased recorded width associated with rotation of

Submitted for publication Aug. 31, 1955.

Aided by a grant from the Muscular Dystrophy Associations of America, Incorporated.

From the Children's Hospital and the Departments of Pediatrics, Radiology, and Research Medicine, University of Pittsburgh School of Medicine.

* Le Gendre, cited by Timme.[20] Fredreich, cited by Ashby and co-workers.[14] Schultze, cited by Timme.[20] References 1-14.

† References 17-19.

Table 1

RADIOLOGIC FINDINGS IN MUSCULAR DYSTROPHY

						LONG BONES				MUSCLES					CHEST	
						UPPER EXTREMITIES		LOWER EXTREMITIES		UPPER EXTREMITIES		LOWER EXTREMITIES				
PATIENT AGE AT ONSET (YR.-SEX)	SKULL	SCOLIOSIS	LORDOSIS	KYPHOSIS	CANINIZATION	OVERTUBULATION OF HUMERUS	RADIUS ULNA	DIVERSITY OF POWER	OVERTUBULATION OF TIBIA-FIBULA	INCREASE SIZE	FAT INFILTRATION	INCREASE SIZE	FAT INFILTRATION	OSTEOPOROSIS	LUNGS	CARDIOTHORACIC RATIO
D.H.-F 7-1	neg.	0	++	0	0	neg.	neg.	val.*	neg.	neg.	neg.	+	0	0	neg.	9/20.1
L.E.-M 13-8	neg.	-	0	-	0	neg.	neg.	neg.	neg.	neg.	+	+	++	0	neg.	11/31.2
R.H.-F 10-10	neg.	+	++	0	0	neg.	neg.	neg.	neg.	neg.	neg.	+	0	0	neg.	9.8/23.8
R.S.-M 5-7	neg.	0	0	0	0	neg.	neg.	val.*	tub.*	?	infil.*	+++	infil.*	0	neg.	9.8/20.2
J.M.-M 9-3	neg.		0		0	tub.*	neg.	val.***	neg.	decr.	infil.*	++	infil.**	1+	neg.	10.0/25.0
T.W.-M 7-8	neg.	0	+	0	0	neg.	neg.	val.*	-	neg.	neg.	++	infil.**	+	neg.	9.4/20.4
W.S.-M 7-10	neg.	-	+	0	0	tub.**	neg.	val.**	neg.	?	?	++	infil.**	+	neg.	prone
G.W.-M 6-8	neg.	0	0	0	0	neg.	neg.	val.*	neg.	neg.	neg.	++	0	0	neg.	8.4/19.8
J.C.-M 5-6	neg.	0	+	0	0	neg.	neg.	val.***	tub.***	neg.	neg.	decr.	infil.**	+	neg.	10.0/22.0
T.W.-M 9-8	neg.	0	+++	0	0	neg.	neg.	val.*	neg.	neg.	neg.	++	0	0	neg.	9.2/22.4
R.S.-M 9-1	neg.	0	0	0	0	tub.*	neg.	val.*	tub.**	neg.	neg.	++	infil.**	0	neg.	prone
L.W.-M 13-8	neg.	0	0	+	0	neg.	neg.	neg.	neg.	?	?	++	infil.**	0	neg.	prone
J.R.-M 10-11	neg.	0	0	++	0	neg.	neg.	val.*	neg.	neg.	neg.	neg.	0	0	neg.	9.3/20.3
E.S.-M 14-8	neg.	0	+++	0	0	neg.	neg.	neg.	neg.	?	infil.**	?	infil.***	0	neg.	12.6/26.5
C.P.-M 7-6	neg.	0	+	+	0	neg.	neg.	val.***	neg.	?	?	+++	infil.***	0	neg.	9.8/22.1
T.H.-M 7-10	neg.	-	-	-	0	tub.**	neg.	val.***	tub.***	+	infil.*	+	infil.*	0	neg.	prone
P.D.-M 5-11	neg.	0	+++	0	+++	tub.***	neg.	val.**	tub.***	decr.	infil.**	decr.	infil.**	+++	neg.	prone
C.S.-M 10-7	thick	0	0	0	+	tub.***	neg.	val.***+	tub.**	?	?	+	infil.*	0	neg.	?
G.Z.-M 8-1	neg.	+	+	0	0	neg.	neg.	val.***	tub.*		infil.**	+	infil.**	0	neg.	prone
W.S.-M 13-4	neg.	-	++	-	0	+++	tub.*	val.**	tub.**	+++	+++	+++	+++	+++	neg.	prone
D.O.-M 15-7	neg.	+++	0	0	++	tub.***	neg.	val.***+	tub.**	?	infil.***	?	infil.***	+++	neg.	prone
J.G.-M 11-1	neg.	0	0	0	0	neg.	neg.	val.**	tub.**	?	?	decr.	infil.**	+	neg.	6.0/22
R.B.-M 10-7	small	+++	+++	0	+++	tub.***	neg.	val.***	tub.***	?	infil.***	?	infil.***	0	neg.	prone
G.P.-M 14-8	small	0	0	0	+++	tub.***	neg.	?	tub.***	+	infil.***	+	infil.***	0	neg.	prone
J.B.-M 3-5	neg.	0	+++	0	+++	tub.***	neg.	val.***+	tub.***	decr.	infil.***	decr.	infil.***	+	neg.	6.0/18
R.J.-M 2-9	neg.	-	+							decr.	infil.***	decr.	infil.***	+++	neg.	prone
D.M.-M 14-10	neg.	**	-	-	**	-	neg.	-	-	?	infil***	?	infil***	+++	neg.	9.3/22.1
A.L.-F 7-9	neg.	+++	+++	0	+	tub.**	neg.	val.***+	tub.**	?	infil.*	?	infil.***	0	neg.	9.4/19.1
C.B.-F 8-6	neg.	+++	+++	+++	0	tub.***	neg.	val.***+	tub.***	decr.	0	decr.	0	+++	neg.	8.2/18
W.S.-M	small	-	-	-	-	tub.**	neg.	val.**	tub.**	+++	infil.***	———	infil.***	+	neg.	prone
E.S.-M	small	-	-	-	-	tub.**		val.**	neg.							

* to include muscle strength

the vertebral bodies. Examples of "caninization" are shown in Figures 1 and 2.

II. Long Bones.—Narrowing or constriction of the shafts of the long bones in absolute terms in relationship to their metaphyses with "trumpet-like" remolding of the metaphyses is called variously overtubulation, overconstriction, overmodulation, or "concentric" narrowing of the long bones. The humerus, femur, tibia, and fibula showed a high incidence of these changes in patients with muscular dystrophy. More marked changes were present in patients with more extensive muscular involvment (Table I).

Fig. 1.—Roentgenograms of the spine in this 6-year-old boy, P. D., show marked lordosis and the changes in the spine that have been called "caninization."

Fig. 2.—This 11-year-old boy, R. B., again shows the lordosis and caninization illustrated in Figure 1.

Bilateral coxa valga deformities were present in most patients. These were most marked in the "far-advanced" group of patients and were sometimes accompanied by neuromuscular subluxation at the hips (Fig. 4). The bones of the forearms were normal roentgenologically.

III. Soft Tissues of the Extremities.—The patients in this group did show increases in the mass of soft tissues of the calves. Large muscle masses without fatty infiltration were present in the early cases. Striation in the

Fig. 3.—Marked overtubulation, or, as it is alternatively known, overconstriction, trumpeting, or remolding, is present in the proximal portion of the humerus of this 13-year-old boy, W. S., with muscular dystrophy. Note the relative hypoplasia of the glenoid fossa.

shadows of the calf muscles indicative of fatty infiltrations was present in the more advanced cases. Abnormal fatty infiltration was present in the soft tissues of the upper extremities and in the thighs in the absence of definite increase in soft tissue mass (Table I). Figures 5, 6, and 7 show examples of fatty infiltrations in the calf and thigh

Fig. 4.—This roentgenograms was taken on the same patient as that shown in Figure 2 and illustrates marked bilateral coxa volga deformities, with subluxation at the left hip.

muscles. Figure 3 shows similar changes in the upper extremities.

IV. Findings in the Remainder of the Radiographic Survey.—Studies of the skull, heart, and lungs showed no roentgen abnormalities. Cariothoracic indices (Table I, final column) were normal.

Bone age estimated according to the methods of Greulich and Pyle was plotted against chronologic age (Fig. 8). Retardation of skeletal maturation was present in the majority of patients, but this is not statistically significant. Osteoporois was pronounced in some patients with severe debility and was probably related to limited activity. This group of patients also had diminished muscle masses, but this does not explain the diminished bone density. Osteoporosis was not present in other patients with comparable muscle wasting.

COMMENT

Tabulation of the roentgen findings reveals that the intensity of changes in patients with muscular dystrophy is related to the extent of the disease as indicated by motor

Fig. 5.—The soft tissue of the calves of the patient, W. B., show marked striation or fatty infiltration.

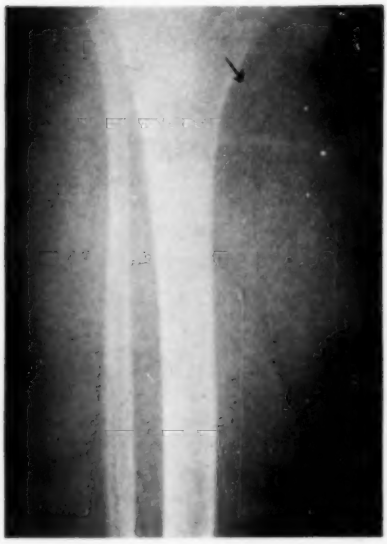


Fig. 6.—Lateral views of calves show the same fatty infiltration evident in the posteroanterior views in Figure 5.

testing of muscle groups. Positive correlation is present between degree of muscular weakness and the incidence and intensity of scoliosis, caninization, overtubulation, coxa valga, neuromuscular subluxation at the hips, fatty infiltration in the muscles, and osteoporosis.

These findings are in keeping with published reports of bone changes in muscular dystrophy based on roentgenograms or postmortem examinations.‡ We have not observed abnormal incidence of some of the changes mentioned in earlier reports, such as pineal calcification § or hypoplasia of the pituitary fossa and sella turcica.[8] In contrast to other reports,‖ hypoplasia of the scapula and glenoid fossa has been infrequent in the group of patients studied here. This is understandable, since hypoplasia of the scapula and glenoid fossa associated with marked overtubulation of the proximal humerus occurs when the disease process affects the upper extremities early. This is not, however, its usual course. Similarly, we have not seen the decrease in the size of the clavicles and ribs [14] or the marrow cavity of long bones ¶ reported by others. Epstein

Fig. 7.—Fatty infiltration is present in the thigh muscles of this 14-year-old boy.

Fig. 8.—Comparison of chronological age and bone age in children with muscular dystrophy. There is a tendency for retardation in that most of the points are above the line which indicates unity. The majority of the points lie, however, within the normal range.

‡ References 1-14 and 20.

§ References 7, 12, and 20.

‖ References 5, 10, 14.

¶ Schultze, cited by Timme.[20] Reference 14.

and Abramson [10] describe widening of medullary cavities and thinning of the cortices of the long bones. Our patients did not show these changes.

Some authors have suggested that the bone changes were congenital in origin and represented mesodermal defects.[10] Shortening of the lower jaw is described to support this view.[11] Shortening of the mandible has not been present in this group of patients. The increased incidence of abnormalities of the skeleton in our group of patients in the more advanced stages of the disease is compatible with a causal relationship with immobilization and disuse.

In our opinion none of the changes save those in the soft tissues of the calves is pathognomonic of muscular dystrophy. Moreover, with this exception all of the changes can be explained on the basis of prolonged disuse. Abnormal fatty infiltration in the increased muscle masses of the calves occurs only in pseudohypertrophic muscular dystrophy.

SUMMARY AND CONCLUSIONS

Radiographic surveys in children with muscular dystrophy have revealed (1) that scoliosis and apparent increase in altitude of the vertebral bodies are more marked and appear more often in patients with the more extensive forms of the disease; lordosis is seen with equal frequency in the early and late stages of the disorder; (2) that valgus deformity of the proximal femurs and neuromuscular subluxation at the hips occur more often in the advanced cases; (3) that the frequency and intensity of the changes in the long bones, consisting of narrowing of the shafts and overtubulation of the metaphyses variously referred to as modulation or overtubulation, are also positively related to the severity and duration of the disease; the bones of the forearm do not participate in these changes; (4) that in the early phases of the disease the calf-muscle masses are increased in size without fatty infiltration being apparent; (5) that striation of soft tissues indicative of infiltration by fat is usually more pronounced in the advanced forms of the disease; in the upper extremities and thighs fatty infiltration may be more evident in the smaller than in the larger muscle masses; (6) that roentgenograms of the skull and chest are not remarkable; bone age is moderately retarded; osteoporosis, when present, is more pronounced in the patients with greatest disabilities.

REFERENCES

1. Gowers, W. R.: Clinical Lecture on Pseudohypertrophic Muscular Paralysis, Lancet **2**:37-39, 1879.

2. Eulenberg, A.: Über einen schweren Fall infantiler, familiärer Muskeldystrophie mit osteoarthropathischen Deformationen, Deutsche med. Wchnschr. **22**:458-460, 1896.

3. Hahn, F.: Über das Auftreten von Contracture bei Dystrophia muscularis progressiva, Deutsche Ztschr. Nervenh. **20**:137-151, 1901.

4. Reference deleted.

5. Spiller, W. G.: Atrophy of Bone in Progressive Muscular Dystrophy, Rev. Neurol. & Psychiat. **3**:388-391, 1905.

6. Tyler, F. H., and Perkoff, G. T.: Studies in Disorders of Muscle: VI. Is Progressive Muscular Dystrophy an Endocrine or Metabolic Disorder? A. M. A. Arch. Int. Med. **88**:175-190 (Aug.) 1951.

7. Janney, N. W.; Goodhart, S. P., and Isaacson, V. I.: The Endocrine Origin of Muscular Dystrophy, Arch. Int. Med. **21**:188-215 (Feb.) 1918.

8. Wright, C.: Consideration of Progressive Muscular Dystrophy with Pseudohypertrophy from an Endocrine Standpoint, California & West. Med. **23**:999-1002, 1925.

9. Hurwitz, S.: Primary Myopathies: Report of 36 Cases and Review of the Literature, Arch. Neurol. & Psychiat. **36**:1294-1316 (Dec.) 1936.

10. Epstein, B. S., and Abramson, J. L.: Roentgenologic Changes in the Bones in Cases of Pseudohypertrophic Muscular Dystrophy, Arch. Neurol. & Psychiat. **46**:868-876 (Nov.) 1941.

11. Maybarduk, P. K., and Levine, M.: Osseous Atrophy Associated with Progressive Muscular Dystrophy, Am. J. Dis. Child. **61**:565-576 (March) 1941.

12. Shank, R. E., Gilder, H., and Hoagland, C. L.: Studies on Diseases of Muscle: I. Progressive Muscular Dystrophy; A Clinical Review of 40 Cases, Arch. Neurol. & Psychiat. **52**:431-442 (Dec.) 1944.

13. Zellweger, H.: Über Knochenveränderungen bei der Dystrophia musculorum progressiva, Ann. paediat. **167**:287-292, 1946.

14. Ashby, D. W.; Williams, G. E. O., and Smith, O. E.: Bone Dystrophy in Association with Muscular Dystrophy (Myopathy), Brit. M. J. **1**: 1486-1488 (June 30) 1951.

15. Lewitan, A., and Nathanson, L.: The Roentgen Features of Muscular Dystrophy, Am. J. Roentgenol. **73**:226-234 (Feb.) 1955.

16. Greulich, W. W., and Pyle, S. I.: Radiographic Atlas of Skeletal Development of the Hand and Wrist Based on the Brush Foundation Study of Human Growth and Development Initiated by T. Wingate Todd, Stanford, Calif., Stanford University Press, 1950.

17. Fetterman, G. H.; Wratney, M. J.; Donaldson, J. S., and Danowski, T. S.: Muscular Dystrophy: I. History, Clinical Status, Muscle Strength, and Biopsy Findings, A. M. A. J. Dis. Child, this issue, p. 326.

18. Danowski, T. S., Greenman, L., Mateer, F. M., Wratney, M. J., and Donaldson, J. S.: Muscular Dystrophy: VII. Trials of a Pituitary Growth Factor, A. M. A. J. Dis. Child., to be published.

19. Donaldson, J. S.; Wratney, M. J.; Pascassio, A.; Weigand, F. A., and Danowski, T. S.: Muscular Dystrophy: VIII. Trials of Protein Hydrolysate, Vitamin Supplements, and Physiotherapy, A. M. A. J. Dis. Child., to be published.

20. Timme, W.: Progressive Muscular Dystrophy as an Endocrine Disease, Arch. Int. Med. **19**:79-104 (Jan.) 1917.

Muscular Dystrophy

III. Serum and Blood Solutes and Other Laboratory Indices

T. S. DANOWSKI, M.D.
P. M. WIRTH
M. H. LEINBERGER, B.S.
L. A. RANDALL
and
J. H. PETERS, M.D., Pittsburgh

It is the general impression that in muscular dystrophy there are no regularly demonstrable abnormalities apart from the often-described changes in creatine and creatinine.* On the other hand, none of the reported observations excluded the possibility of significant mean deviations detectable only upon comparison with suitable control groups. That this is indeed so is evident from studies presented in this paper.

Submitted for publication Aug. 31, 1955.

From the Department of Research Medicine, Children's Hospital, University of Pittsburgh School of Medicine.

Supported by grants-in-aid from the Muscular Dystrophy Associations of America, Incorporated, The United States Public Health Service, and the American Cancer Society (Martha O. Freas Estate).

Present address of Dr. Peters: U. S. Veterans' Hospital, Atlanta, Ga.

MATERIAL AND METHODS

The following observations were made in a group of 31 children with history, physical examination, muscle biopsy, spinal fluid findings, and radiologic features compatible with the childhood type of muscular dystrophy.†

A. Creatine Tolerance Tests.—Serum levels of creatine and creatinine were determined prior to and following the oral administration of creatine‡ to children with muscular dystrophy and to healthy controls on the per-kilogram-of-body-weight dosage schedule indicated in Figure 2.

* References 1-7.
† References 8 and 9.
‡ References 10 and 11.

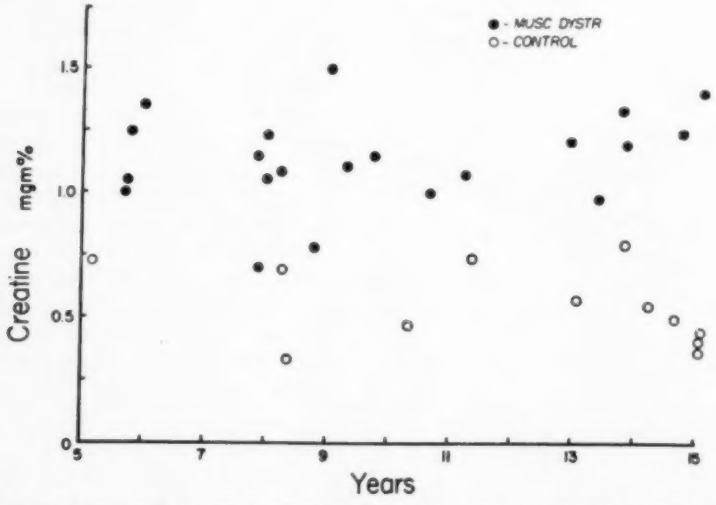


Fig. 1.—Fasting creatine levels in muscular dystrophics compared to those in normal children. It is readily evident that fasting serum creatine levels are higher in muscular dystrophy.

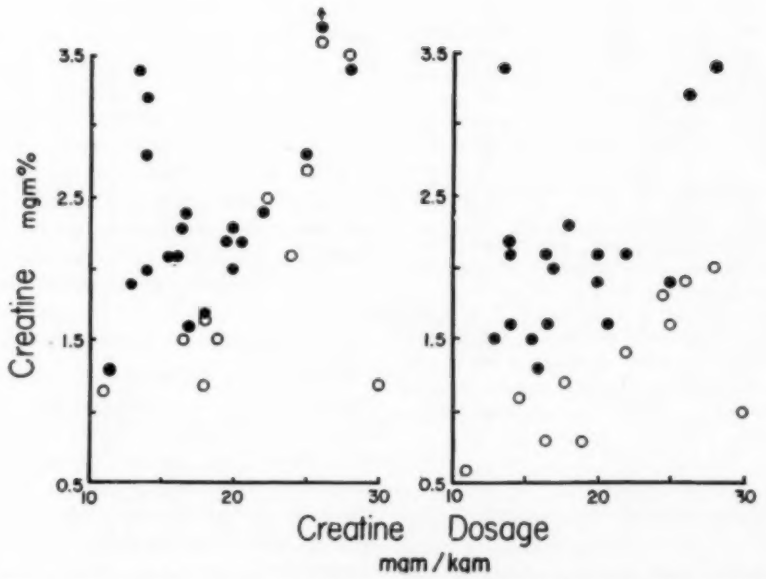


Fig. 2.—Changes in serum creatine following the oral administration of creatine to children with muscular dystrophy and to normal controls. It is evident that 45 minutes after the injection of creatine in the per-kilogram dosage indicated in the Figure that no sharp distinction exists between the dystrophic and the control subjects. However, at 135 minutes a definite separation of the two groups appears, since at any particular dosage level the controls show less hypercreatinemia than the children with muscular dystrophy.

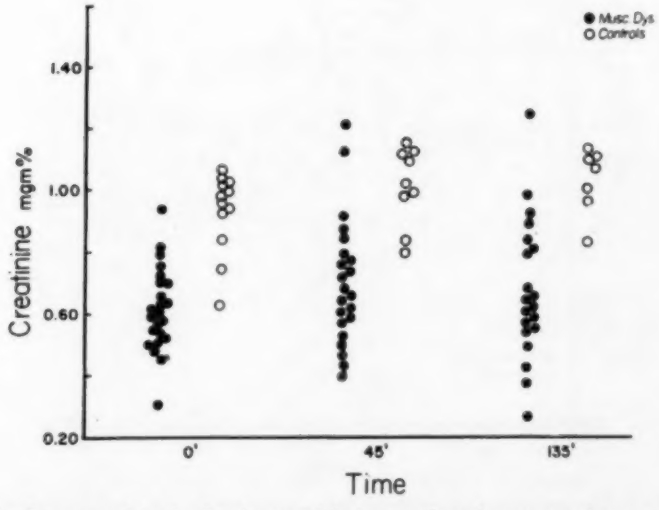


Fig. 3.—Serum creatinine levels prior to and during creatine tolerance tests in normal children and in patients with muscular dystrophy. The children with muscular dystrophy have lower levels of creatinine. The administration of creatine raises the creatinine level. This may represent contamination of administered creatine with creatinine.[27]

B. Blood and Serum Solutes.—Fasting levels of blood sugar and nonprotein nitrogen and of serum chloride, sodium, potassium, calcium, phosphorus, total protein, albumin, globulin, cholesterol, and total carbon dioxide content were measured by analytic methods in use in this laboratory and compared with the findings in healthy children of the same age.[13] The control studies were conducted in a well-run private institution with careful duplication of the experimental conditions.

C. Hematologic, Urine, and Liver Studies.—Blood cell count, hematocrit, sedimentation rate, erythrocyte fragility, bleeding, clotting and clot retraction times, urinalyses, P. S. P. excretion, B. S. P. excretion, prothrombin time, thymol turbidity, cephalin flocculation, and alkaline phosphatase levels were obtained, in addition to the determination of serum protein, albumin, globulin, and cholesterol levels cited earlier.

RESULTS

A. Creatine Tolerance Tests.—From Figure 1 it is readily evident that as a group these children with muscular dystrophy had fasting levels of creatine in serum which were generally higher than those present in healthy children of the same age. The administration of creatine by mouth in the per-kilogram dosage indicated in Figure 2 produced hypercreatinemia. At the 45-minute point this was often of comparable degree in the dystrophic and nondystrophic children. At 135 minutes, however, a definite separation of the two groups is evident, with a relative hypercreatinemia present in the children with muscular dystrophy. Fasting creatinine levels, on the other hand, were in general higher in the nondystrophy control children and tended to rise in both groups during the creatine tolerance (Fig. 3).

B. Blood and Serum Solutes.—Upon comparison of muscular dystrophy patients with a group of healthy children, serum total CO_2 content and sodium, potassium, total protein, albumin, and globulin levels are of the same orders of magnitude in the two groups. The same statement applies to the fasting levels of venous whole blood nonprotein nitrogen and sugar.

On the other hand the data in Figures 4, 5, 6, and 7 indicate that the mean levels

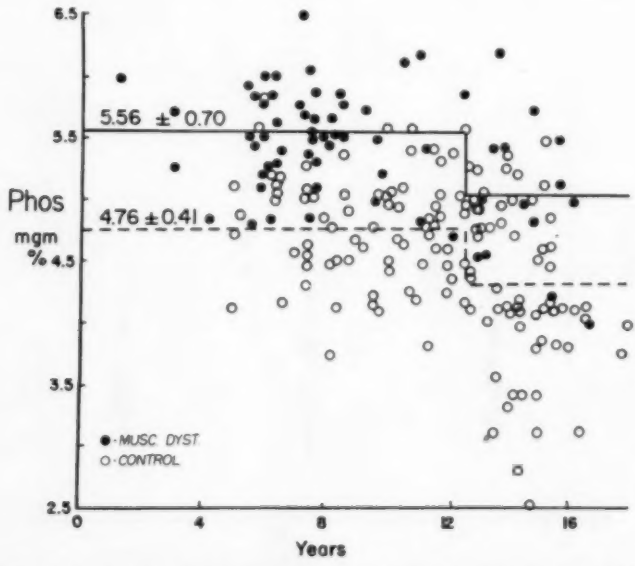


Fig. 4.—Serum inorganic phosphorus in muscular dystrophy and in control children. The closed circles represent muscular dystrophy patients. Comparison of the mean value in this group with the average obtained in a larger group of normals (open circles), boys and girls from a children's home, indicates that on the average serum inorganic phosphorus values are higher in muscular dystrophy.

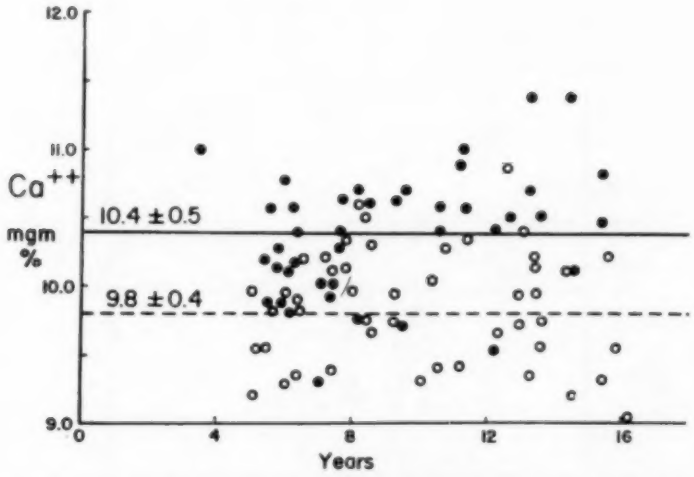


Fig. 5.—Concentrations of serum calcium in muscular dystrophy and in control children. As in the case of the serum inorganic phosphorus, children with muscular dystrophy (closed circles) have a higher calcium level than that recorded in control observations in normal boys and girls (open circles). This difference is statistically significant, with *P*-value of less than 0.0001.

of serum inorganic phosphorus and calcium are higher and those of chloride and cholesterol are lower in muscular dystrophy patients. These differences are statistically significant (*P*-values of 0.01 to less than 0.001). There is no evidence that these differences are more prevalent or marked in the far-advanced cases. In the case of calcium this possibility has been tested by comparing patients with minimal and early involvement

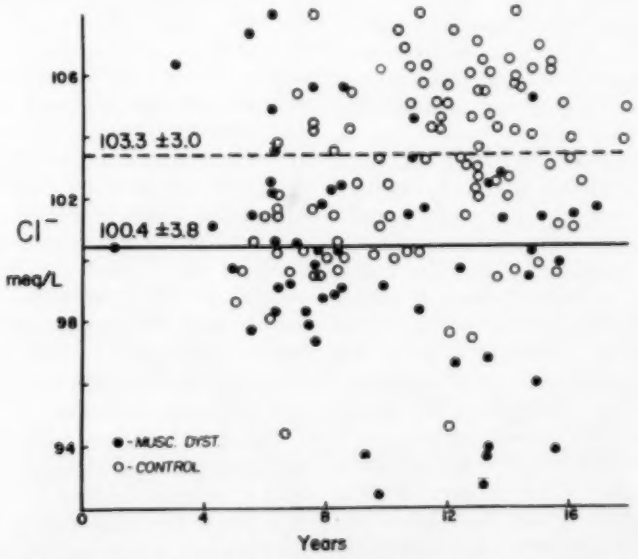


Fig. 6.—Serum chloride values in muscular dystrophy. Observations on normal children (open circles) yielded a mean value of 103.0 mEq/liter, in contrast to an average of 100.4 in the muscular dystrophy patients (closed circles) represented in this Figure (*P*-value less than 0.0001).

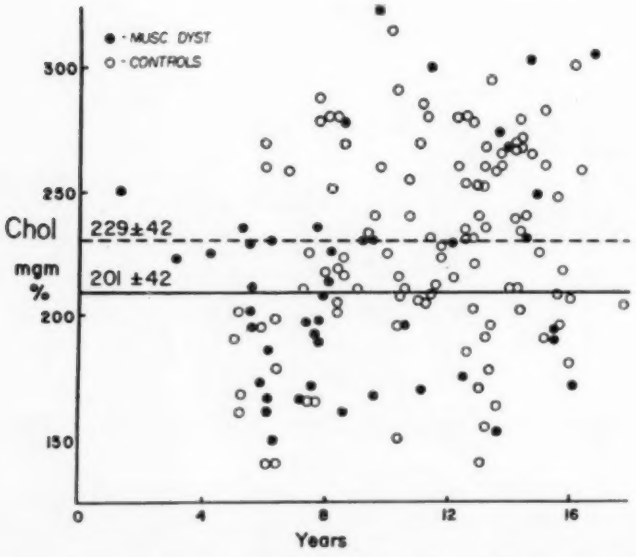


Fig. 7.—Comparison of cholesterol values in the sera of patients with muscular dystrophy and in normal controls. The mean value of 209 mg. per 100 cc. in the muscular dystrophy group (closed circles) herein presented is somewhat lower than the average cholesterol in normal children.

with those who were far advanced (Fig. 8) and checking the degree of osteoporosis as reported in previous studies[9] against the calcium level (Fig. 9).

C. Hematologic, Urine, and Liver Studies.—Erythrocyte, leucocyte, and differential counts of the peripheral blood cells were not remarkable in this group of patients. The hematocrit readings ranged from 30 to 51 vol. %, with a mean value of 38.8; the sedimentation rates proved to be 3 to 16 mm. in one hour, with only two higher values, 20 and 29, in two of the patients; with but one exception, erythrocytes began to hemolyze in hypotonic saline solutions of 0.42% to 0.48%, with completion of the process at 0.30% to 0.35%. Bleeding (1.3 to 2.8 minutes), coagulation (4.0 to 8.0 minutes), and clot-retraction times (1 to 12 hours) were not remarkable. The reticulocytes varied between 0.1% and 0.8%, with levels of 2.0% and 1.8% in two of the children. Fasting eosinophile counts ranged from 13 to 331 cells per cubic millimeter.

Insofar as renal status was concerned, the children with muscular dystrophy concentrated to specific gravities of 1.023 to 1.036 without previous restriction of fluids. There was no glycosuria. As indicated earlier the whole blood N. P. N. values were within the normal range. The majority of patients showed a 1+ albuminuria at one time or another, and in three of them a 2+ albuminuria was present. This was not associated with either erythrocytes, leucocytes, or casts in the sediment, nor was the excretion of P. S. P. dye impaired. If anything, the latter appeared to be above normal, with eight of the children returning between 80% and 100% of the injected dye. In two of the patients the specimen voided between the second and fourth hours contained 20% of the dye. This points to incomplete emptying of the bladder but does not establish that it was involuntary retention.

The studies of liver function did not unearth any definite or consistent abnormalities. B. S. P. retention at 30 or 45 minutes ranged from 0% to 6% following a dosage of 5 mg. per kilogram of body weight. The prothrombin time usually agreed very closely with that determined simultaneously in control

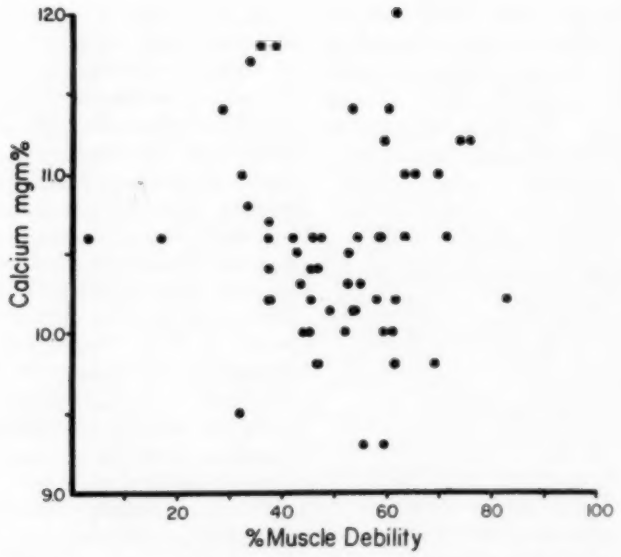


Fig. 8.—Comparison of muscle debility with serum calcium level. It is obvious that the relative hypercalcemia was present with equal frequency irrespective of the degree of muscle involvement.

subjects. The cephalin flocculation test was usually 1+ at 24 and again at 48 hours, an insignificant value, with one instance, A. L., of 2+ at 48 hours. Thymol turbidity was found to be 0.5 to 1.5 MacLaglan units, total bilirubin was 0.5 to 0.7 mg. per 100 cc., and the alkaline phosphatase varied between 0.8 and 6.0 Bodansky units, though one patient, E. F. S., had a level of 11.3 units. As already noted, the total protein, albumin, and globu-

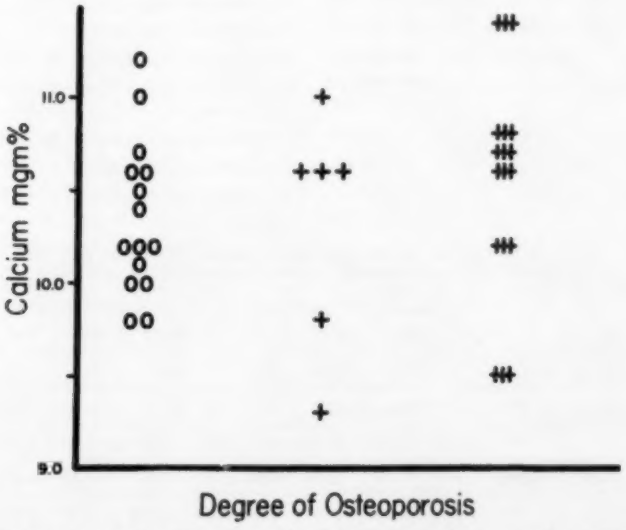


Fig. 9.—Osteoporosis and serum calcium levels in muscular dystrophy. In these 12 patients osteoporosis was present with equal frequency irrespective of the serum calcium level.

lin values were not detectably different in the muscular dystrophics, whereas the serum total cholesterol concentrations were relatively lower. In fact, fasting levels of more than 1.25 mg. per 100 cc. are not common in any other group of patients that we have had occasion to study.§

COMMENT

The creatine studies confirm the findings of others [15] that in muscular dystrophy fasting serum levels are considerably higher than those in control groups. As has been noted in other conditions,[11] the degree of elevation observed 45 minutes after creatine administration is extremely variable, and there is no clear distinction between normals and patients with decreased tolerance.

After 135 minutes, however, the two groups are clearly distinguished by persistence of the elevated serum concentrations in the dystrophic group. This is in keeping with the data obtained by Cummings, using a different technique,[15] and was to be expected in view of the decreased tolerance previously demonstrated by others who have measured urine creatine under similar circumstances.|| Although as yet only indirect evidence obtained by observation of the effects of N^{15} glycine administered to dystrophic males is available, this intolerance is apparently attributable to reduced muscle uptake.[19]

The low levels of serum creatinine have been previously noted by others ¶ and undoubtedly account for the relatively small amounts of urinary creatinine which have long been recognized as being typical of this condition.# This view is in keeping with studies in normal subjects.* It is possible that the small increases in serum creatinine following creatine ingestion were the result of contamination of administered creatine by small amounts of creatinine.[27] However, concurrent protocols on adults during the period of these studies indicate that the changes in creatinine were not contamination errors. Some elevation of creatinine following creatine administration is quite consistent with the evidence adduced by Benedict and her associates [28] that creatine-creatinine conversion rates are increased in dystrophic individuals.

Careful comparison of serum constituents in this group and in normal children does reveal differences in the mean values of serum inorganic phosphorus, calcium, and cholesterol. These are not correlated in degree with the intensity of the disease. Review of published reports indicates that in the Hurwitz series of 36 cases [29] hyperphosphatemia and hypercalcemia of the degree noted in ours was encountered without comment. Tyler and Perkoff's data include serum phosphorus and cholesterol values in the normal range, but they were apparently not statistically

§ References 10-12.

|| References 16-18.

¶ References 14, 15, and 20.

References 21 and 22.

* References 22-26.

FASTING LEVELS OF SERUM AND BLOOD CONSTITUENTS IN CHILDREN WITH MUSCULAR DYSTROPHY COMPARED TO HEALTHY CHILDREN

	Muscular Dystrophy Mean ± S.D. (#)	Healthy Children Mean ± S.D. (#)
HCO_3 (mEq/l)	22.6 ± 2.8 (49)	23.1 ± 1.3 (125)
Na "	143 ± 3.0 (48)	144 ± 3.0 (106)
K "	4.48 ± 0.39 (52)	4.37 ± 0.40 (142)
Prot. (gm%)	7.17 ± 0.68 (48)	7.27 ± 0.57 (49)
Alb. "	4.38 ± 0.57 (48)	4.28 ± 0.58 (47)
Glob. "	2.79 ± 0.56 (48)	3.00 ± 0.55 (47)

compared with a control series.[6] The average of the phosphorus values they obtained in patients less than 12 years old was 5.2 mg. per 100 cc., and therefore above the average in our healthy children.

Similarly, it appears probable that relative hypochloremia and hypocholesterolemia were also present in both of the series cited, though the observations were limited in number and control data are not available for comparison. In addition, McCrudden and Sargent [30] have reported an isolated instance of hypocholesterolemia.

As Dreyfus and Schapira [31] have pointed out, the hypocholesteremia is one of the several important respects in which human dystrophy differs sharply from nutritional dystrophy in animals, since, as Morgulis and Spencer have shown,[32] cholesterol values are consistently found to be elevated in vitamin-E-deficient rabbits.

Only limited speculation is possible concerning the origins of these abnormalities. Balance studies on two patients reported by Milhorat and Toscani showed retention of calcium on a low intake in one.[33] It is possible that the higher calcium values reflect some anomaly of serum proteins resulting in greater calcium binding. If this be so, then it is present without gross change in the levels of the serum protein fractions. The higher calcium values are not attributable to increased intake of vitamin D, since no such histories were obtained. Neither would parathyroid activity explain the relative hypercalcemia, since the phosphate levels were not depressed and renal failure was not present. It may be that they reflect relative immobilization and osteoporosis, since equally high calcium values have been found in uncomplicated old age and in children with residual paralysis following anterior poliomyelitis †.

Insofar as the relative hyperphosphatemia is concerned, it is conceivable that this merely reflects a delay in the biochemical maturation which results in a lowering of serum inorganic phosphorus levels with progressive growth in children.‡ This of course only draws a parallel and does not explain the origins of this change. It may be suggested that growth hormone plays a role, since in active acromegaly or giantism high levels of inorganic phosphorus are encountered.[34] On the other hand, no such stigmata are found in this entity. Other causes of relative or absolute hyperphosphatemia, such as renal failure, hypoparathyroidism, and rickets, are untenable in view of the lack of other confirmatory findings. It is possible but unestablished that the creatine intolerance and high phosphorus values are interrelated, since a complex of creatine-phosphate is formed in muscle. Similarly, the work of Tyler and Perkoff [6] and of Van Bekkum and Querido [35] suggests that the muscular dystrophic does not show the decreases in serum inorganic phosphorus characteristic of healthy subjects during the disposal of exogenous carbohydrate. This is attributed to a decrease in the muscle mass which can participate in phosphorylation and glycolysis.

The chloride differences are not reflected in the bicarbonate levels. Their origin is unknown. It should be pointed out that on a protein-hydrolysate-vitamin regimen which provided extra chloride, this difference between healthy children and patients with muscular dystrophy disappeared.[36]

Insofar as the somewhat lower cholesterol levels are concerned, their origin is also unknown. They are not attributable to liver disease; other studies [37] indicate that in general thyroid function is unimpaired, but this is not certain. It may be that they are a concomitant of malnutrition, referring only to muscles, but drawing an analogy with general undernutrition which results ultimately in lowering of cholesterol levels. The diet of these youngsters is not low in fat, and hence this cannot be advanced as an explanation for the lowered cholesterol levels. It should be pointed out that the possibility of a primary disorder of fat metabolism

† Danowski, T. S.: Age and Sex Differences in the Solutes of Fasting Serum and Blood, unpublished data.

‡ Danowski, T. S.: Age and Sex Differences in the Solutes of Fasting Serum and Blood, unpublisted data.

exists in that in no other condition save possibly arthrogryposis [35] does the parallel of decreasing muscle mass and overproduction of tissue fat coexist so regularly. Finally, it should be pointed out that these differences also disappeared during therapy with protein hydrolysate and supplementary vitamins.[35]

Hematologic, renal, and hepatic studies did not uncover any consistent defect or change; the high P. S. P. excretion may point to reduced destruction of intramuscularly injected dye. The regularity with which 1+ cephalin flocculation was encountered is in keeping with the findings in normals and was not accompanied by any change in the other liver indices.

SUMMARY AND CONCLUSIONS

A detailed survey has been undertaken of a number of children with the childhood form of muscular dystrophy as indicated by the history, physical findings, negative spinal fluid examination, loss of muscle strength, results of muscle biopsy, and presence of relative hypercreatinemia and creatine intolerance. Formed elements of blood and various hematologic studies did not uncover any persistent abnormalities; studies of kidney and liver function were generally negative, though high P. S. P excretion and 1+ cephalin flocculation were at times present.

On the other hand, careful comparison of serum phosphorus and calcium values with those in healthy children reveals a relative increase in muscular dystrophy; in contrast, cholesterol and chloride values are somewhat lower. There is no one explanation that can be advanced to account for these recorded differences, though a variety of possibilities have been mentioned. Concentrations of all other serum and blood solutes measured were of comparable orders of magnitude in the dystrophic and nondystrophic groups.

REFERENCES

1. Nevin, S.: Primary Diseases of Voluntary Muscles, J. Neurol. & Psychiat. **1**:120-141 (April) 1938.

2. Milhorat, A. T.: Treatment of Diseases of Muscle, New York J. Med. **42**:2210-2214 (Dec. 1) 1942.

3. Viets, H. R., and Brown, M. R.: Medical Progress: Diseases of Muscles, New England J. Med. **245**:647-653 (Oct. 25) 1951.

4. Tyler, F. H., and Wintrobe, N. M.: Studies in Disorders of Muscle: I. Problem of Progressive Muscular Dystrophy, Ann. Int. Med. **32**:72-79 (Jan.) 1950.

5. Tyler, F. H., and Stephens, F. E.: Studies in Disorders of Muscle: IV. The Clinical Manifestations and Inheritance of Childhood Progressive Muscular Dystrophy, Ann. Int. Med. **35**:169-185 (July) 1951; Correction **35**:1164 (Nov.) 1951.

6. Tyler, F. H., and Perkoff, G. T.: Studies in Disorders of Muscle: VI. Is Progressive Muscular Dystrophy an Endocrine or Metabolic Disorder? A. M. A. Arch. Int. Med. **88**:175-190 (Aug.) 1951.

7. Denny-Brown, D.: Nature of Muscular Diseases, Canad. M. A. J. **67**:1-6 (July) 1952.

8. Fetterman, G. H.; Wratney, M. J.; Donaldson, J. S., and Danowski, T. S.: Muscular Dystrophy: I. History, Clinical Status, Muscle Strength, and Biopsy Findings, A. M. A. J. Dis. Child., this issue, p. 326.

9. Girdany, B. R., and Danowski, T. S.: Muscular Dystrophy: II. Radiologic Findings in Relation to Severity of Disease, A. M. A. J. Dis. Child., this issue, p. 339.

10. Peters, J. H.: The Determination of Creatinine and Creatine in Blood and Urine with the Photoelectric Colorimeter, J. Biol. Chem. **146**:179-186 (Nov.) 1942.

11. Peters, J. H.; Schwartz, R.; Mermelstein, H. A.; Nefores, M. N., and Mansuy, M. M.: Studies of Serum Creatine Tolerance: I. Findings in Normal Males and in Hyperthyroidism, J. Clin. Invest. **30**:799-808 (Aug.) 1951.

12. Peters, J. H.; Snyderman, R., and Crutcher, J. C.: Role of Female Genital Function in Creatine Metabolism as Revealed by the Serum Creatine Tolerance Test, Am. J. Med. **19**:149, 1955.

13. Danowski, T. S.; Greenman, L.; Mateer, F. M.; Parsons, W. B.; Weigand, F. A.; Mermelstein, H. A., and Peters, J. H.: Carboxylic Cation Exchange Resin Effects in Dogs, J. Clin. Invest. **30**:984-994 (Sept.) 1951.

14. Janney, N. W.; Goodhart, S. P., and Isaacson, V. I.: The Endocrine Origin of Muscular Dystrophy, Arch. Int. Med. **21**:188-215 (Feb.) 1918.

15. Cummings, J. N.: Creatine and Guanidoacetic Acid Metabolism in Muscle Disease, Brain **76**:299, 1953.

16. Milhorat, A. T., and Wolff, H. G.: Metabolism of Creatine and Creatinine in Muscle Disease, Ann. Int. Med. **9**:834-837 (Jan.) 1936.

17. Milhorat, A. T., and Wolff, H. G.: Studies in Diseases of Muscle: II. Effect of Varying Amounts of Ingested Creatine on Creatine Tolerance in Progressive Muscular Dystrophy, Arch. Neurol. & Psychiat. **39**:37-40 (Jan.) 1938.

18. Hoagland, C. L.; Gilder, H., and Shank, R. E.: Synthesis, Storage and Excretion of Creatine, Creatinine, and Glycocyamine in Progressive Muscular Dystrophy, and the Effects of Certain Hormones on These Processes, J. Exper. Med. **81**: 423-438 (May) 1945.

19. Roche, M.; Benedict, J. D.; Uy, T. F.; Bien, E. J., and Stetten, DeW., Jr.: Origin of Urinary Creatine in Progressive Muscular Dystrophy, Metabolism **1**:13-19 (Jan.) 1952.

20. Mosberg, G.: Beitrag zur Kenntnis des Stoffwechsels der Dystrophia musculorum progressiva, Klin. Wchnschr. **9**:2051-2052 (Nov. 1) 1930.

21. Hunter, A.: Creatine and Creatinine, New York, Longmans, Green and Co., Ltd., 1928.

22. Chanutin, A.: The Fate of Creatine When Administered to Man, J. Biol. Chem. **67**:29-41 (Jan.) 1926.

23. Rose, W. C., and Dimmitt, F. W.: Experimental Studies on Creatine and Creatinine: VII. The Fate of Creatine and Creatinine When Administered to Man, J. Biol. Chem. **26**:345-353 (Sept.) 1916.

24. Bloch, K., and Schoenheimer, R.: Studies in Protein Metabolism: XI. The Metabolic Relation of Creatine and Creatinine Studied with Isotopic Nitrogen, J. Biol. Chem. **131**:111-119 (Nov.) 1939.

25. Borsook, H., and Dubnoff, J. W.: The Hydrolysis of Phosphocreatine and the Origin of Urinary Creatinine, J. Biol. Chem. **168**:493-510 (May) 1947.

26. Hoberman, H. D.; Sims, E. A. H., and Peters, J. H.: Creatine and Creatinine Metabolism in the Normal Male Adult Studied with the Aid of Isotopic Nitrogen, J. Biol. Chem. **172**:45-58 (Jan.) 1948.

27. Cameron, J. D. S.: The Effect of Oral Administration of Creatinine on Blood and Urine, Quart. J. Exper. Physiol. **23**:351-366, 1923.

28. Benedict, J. D.; Kalinsky, S. J.; Scarrone, L. A.; Werthein, A. R., and Stetten, DeW., Jr.: The Origin of Urinary Creatine in Progressive Muscular Dystrophy, J. Clin. Invest. **34**:141-145 (Jan.) 1955.

29. Hurwitz, S.: Primary Myopathies: Report of 36 Cases and Review of the Literature, Arch. Neurol. & Psychiat. **36**:1294-1316 (Dec.) 1936.

30. McCrudden, R. H., and Sargent, C. S.: Hypoglycemia and Progressive Muscular Dystrophy, Arch. Int. Med. **17**:465-475 (April) 1916.

31. Dreyfus, J. C., and Schapira, G.: Les Syndromes biochimiques musculaires, in Le Muscle: Étude de biologie et de pathologie, Moulins, Crepin-Leblond & Cie, 1950, p. 357.

32. Morgulis, A., and Spencer, H. C.: Studies on the Blood and Tissues in Nutritional Muscular Dystrophy, J. Nutrition **12**:173-190 (Aug.) 1936.

33. Milhorat, A. T., and Toscani, V.: Studies in Diseases of Muscle: VIII. Metabolism of Calcium, Phosphorus and Magnesium in Progressive Muscular Dystrophy, Myotonia Atrophica and Familial Periodic Paralysis, Arch. Neurol. & Psychiat. **41**: 1130-1137 (June) 1939.

34. Li, C. H.; Geschwind, I., and Evans, H. M.: Effect of Growth Hormone on Inorganic Phosphorus Levels in Plasma, Endocrinology **44**:67-70 (Jan.) 1949.

35. Van Bekkum, D. W., and Querido, A.: Inorganic Phosphate Response to Intravenous Glucose Administration in Progressive Muscular Dystrophy, J. Clin. Invest. **32**:1061-1064 (Nov.) 1953.

36. Donaldson, J. S.; Wratney, M. J., Pascassio, A., Weigand, F. A., and Danowski, T. S.: Muscular Dystrophy: VIII. Trials of Protein Hydrolysate, Vitamin Supplements, and Physiotherapy, A. M. A. J. Dis. Child., to be published.

37. Danowski, T. S.; Leinberger, M. H.; Wirth, P. M.; Mateer, F. M., and Greenman, L.: Endocrine Studies in Muscular Dystrophy, to be published.

38. Lewitan, A., and Nathanson, L.: The Roentgen Features of Muscular Dystrophy, Am. J. Roentgenol. **73**:226-234 (Feb.) 1955.

Muscular Dystrophy

IV. Endocrine Studies

T. S. DANOWSKI, M.D.
R. M. BASTIANI
F. D. McWILLIAMS
F. M. MATEER, M.D.
and
L. GREENMAN, M.D., Pittsburgh

Despite early opinion to the contrary, it is now agreed that in muscular dystrophy there are no gross endocrinologic abnormalities. Evaluation of a group of children with muscular dystrophy undertaken in this clinic * provided us with an opportunity to determine the endocrine status of such children by means of some of the newer indices.

MATERIAL AND METHODS

Data based on observations in some but not all the members of a group of 31 children with muscular dystrophy are available. The clinical status of each child, the findings on biopsy of muscles, and the results of roentgenographic, hematologic, blood, serum, urine, and liver studies have been reported in the studies cited earlier †; relative hypercreatinemia was present prior to and at the 145-minute point of creatine tolerance tests. The particular endocrine studies, the techniques employed, and the findings are presented in the section which follows.

RESULTS

A. Pituitary Gonadotropins.—The output of gonadotropins in a 24-hour period (Table I) estimated from changes in the ovaries and uterus, hyperemia and weight, of immature mice on the fourth day following injection of residue from ultrafication of urine,[5] falls within the range reported to exist in healthy children of the same age.[6]

B. Indices of Thyroid Activity.—Basal metabolic rate measurements calculated with the aid of standard body weight-height-surface area formulae showed a scatter of values above and below normal. These ranged from —30 to +51 in 22 patients, with a mean value of +19.6% (Table II). Tachycardia at rest, previously noted by others.‡ was a frequent finding in our patients during the B. M. R. determination as well as at other times. As already mentioned in the previous paper,[8] fasting serum cholesterol values were lower on the average in muscular dystrophy than those found in a group of healthy children. On the other hand, there is no correlation between the B. M. R. and the level of cholesterol in the group of muscular dystrophy children listed in Table II.

Furthermore, the serum protein-bound iodine level, which has proved to be a sensitive reflection of the level of thyroid function,[14] was of a different order of magnitude in the two groups (Fig. 1). In general the children with muscular dystrophy had protein-bound iodine values above those in the normal children. In addition it is to be noted that several of the muscular dystrophy children had concentrations above the usual euthyroid limit of 7.5γ per 100 cc.

The disposal of exogenous thyroxin given at one time per os on a body weight basis, 0.2 mg. per kilogram, was studied by means of serial protein-bound iodine measurements in six of the children with muscular dystrophy. These patients have been included in an earlier report from this laboratory.[15]

Submitted for publication Aug. 31, 1955.

Established Investigator, American Heart Association (Dr. Mateer).

From the Children's Hospital and the Department of Research Medicine, University of Pittsburgh School of Medicine.

Supported by grants-in-aid from the Muscular Dystrophy Associations of America, Incorporated, the United States Public Health Service, and the Atomic Energy Commission.

* References 1-4.

† References 1-4.

‡ References 7-13.

Table I

URINARY GONADOTROPIN EXCRETION IN MUSCULAR DYSTROPHY

Patient Age-Sex	24-Hr. Urine Volume (ml.)	Mouse Units					
		3.3	6.6	13.0	26.0	53.0	106.0
D.H. 7 F	525	-	-	-	-	-	
L.K. 14 M	580		-	-	-	-	-
B.H. 11 F	570	-	-	-	-	-	
E.S. 15 M	270		-	-	-	-	-
J.M. 9 M	375		-	-	-	-	-
T.W. 8 M	120		-	-	-	-	-
D.E. 7 M	200	-	-	-	-	-	
W.S. 7 M	520	-	-	-	-	-	-
J.C. 6 M	230			-	-	-	-
T.M. 10 M	330		±	-	-	-	-
H.S. 8 M	240	-	-	-	-	-	
L.W. 14 M	470		±	-	-	-	-
J.R. 10 M	600	-	-	-	-	-	
E.S. 16 M	610		+	+	±	-	-
C.P. 8 M	520		-	-	-		
T.H. 8 M	130	-	-	-	-	-	
P.D. 6 M	400	-	-	-	-	-	
C.K. 11 M	2300	-	-	-	-	-	
G.Z. 9 M	260		-	-	-	-	-
W.S. 13 M	600		-	-	-	-	-
D.D. 16 M	300		+	+	±	-	-
J.O. 11 M	240		±	-	-	-	-
R.B. 11 M	260		-				
G.P. 15 M	500		-to±	-	-		
D.M. 13 M	480		+	±	-		
A.L. 8 F	670		-	-	-	-	
C.B. 9 F			-	-	-		
E.S. 9 M	400		-	-			
W.S. 9 M	400		+	+	+	-	-

The findings in this group are compared with those in healthy nonhospitalized children in Fig. 2. The rate of disappearance of exogenous thyroxin was of the same order of magnitude in the two groups of subjects.

C. Serum Calcium and Phosphorus.—In the preceding paper [3] it was pointed out that the mean values of serum inorganic phosphorus and of calcium were higher in children with muscular dystrophy than in control subjects of comparable age (5.56 versus 4.76, and 10.4 versus 9.8 mg. per 100 cc., respectively.

D. Gonads and Adrenal Cortices.—The urinary output of 17-ketosteroids shown in Figure 3 fell within normal limits.* Urinary

* References 6, 16, and 17.

Table II

INDICES OF THYROID FUNCTION IN MUSCULAR DYSTROPHY

Patient	Height (cms)	Weight (kg)	B.M.R. Pulse rate Maximum	Minimum	B.M.R. (%)	Serum Cholesterol (mgm%)	Serum PBI (%)
D.H.	117	22.0	110		+ 7	166	5.1
L.K.		58.7	88	94		276	6.2
B.H.	152	34.0	96	90	+ 6	170	5.3
E.S.	112	20.5 20.5	104	104	+25 +13	211	6.3
J.M.	128	23.2	80	80	13	231	6.3
T.W.	119	21.8	88	88	+11	188	6.3
D.E.	126	22.0	88	80		198	6.9
W.S.	115	22.0	100	100	+23	207	5.5
J.C.	110	18.1	100	100	+ 8	200	6.6
T.M.	164	25.3	80	76	-10	230	7.0
H.S.	120	22.6	88	90	+28	213	5.9
L.W.		20.0	98			153	6.4
J.R.	126	19.3	98	98	+45	183	7.5
E.S.	169	70.9	66	66	+ 7	304	4.7
C.P.	123	23.1	82	82	+28	171	6.3
T.H.	124	20.0	80	76		236	8.0
P.D.	98	15.9	108	102	+27	173	5.9
C.K.	150	25.0	102	100	+22	229	7.8
G.Z.	96	28.6	104	106	+26 +31	225	6.0
W.S.	150	55.0	94	90		270	7.1
D.D.		62.0	96	88		190	19.4
J.O.	126	22.7	104	102	+ 1	200	6.1
R.B.	144	39.2	88	88		194	
G.P.	155	50.9	96	96	+ 3	196	21.3
D.M.	119	19.0	108	108	+32	173	7.0
A.L.	108	16.5	100	100	+ 1	198	6.0
W.L.	121	18.7	84	76	+51	178	6.2
E.S.	150	56.9	100	100	-25	167	9.3
W.S.	168	79.9	98	100	-30	176	10.0

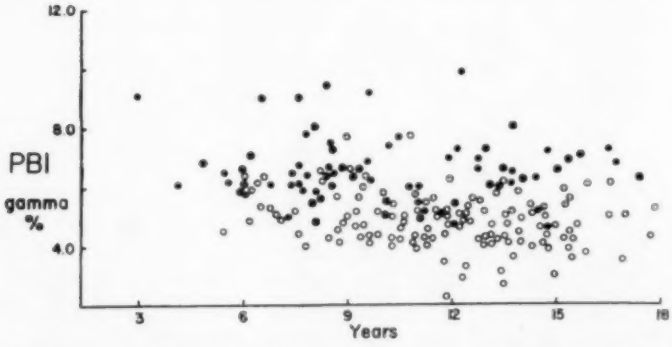


Fig. 1.—Comparison of serum protein-bound-iodine concentrations in muscular dystrophic and in normal children. The open circles, referring to healthy boys and girls from a home for children, all fall below 8γ per 100 cc. and, with but two exceptions, below 7γ per 100 cc. It is to be noted that in the pubescent-adolescent age group there are a number of values below 4 and even below 3γ per 100 cc. This has been noted previously as a pronounced manifestation of growth and development.[14]

The children with muscular dystrophy (solid circles) were found on repeated examinations to have serum protein-bound-iodine values that were in the upper half of the normal range or actually above it. There is a suggestion that during the pubescent-adolescent age period the iodine values are also lower in this group, as they are in the control children.

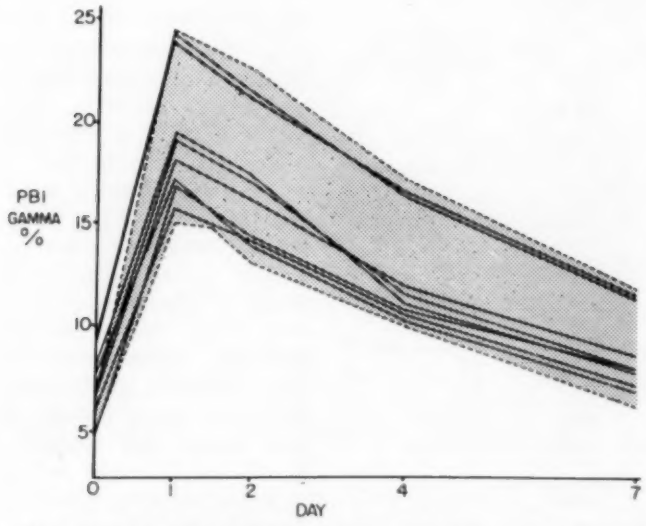


Fig. 2.—Disposal of exogenous thyroxin in muscular dystrophy. The shaded background indicates the results of serial measurements of serum protein-bound iodine in normal children given 0.2 mg. of *l*-thyroxine by mouth at zero time; solid lines identify patients with muscular dystrophy. It is obvious that the rate of disposal of exogenous thyroxin is of the same order of magnitude in the two groups of patients.

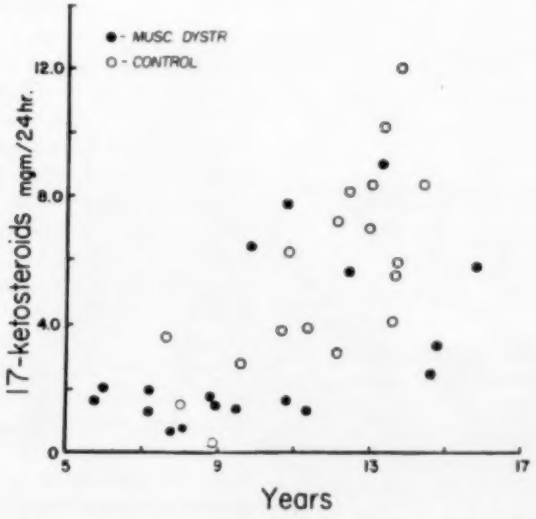


Fig. 3.—Urinary excretion of 17-ketosteroids in muscular dystrophy and in control children. It is evident from the Figure that children with muscular dystrophy (solid circles) excrete 17-ketosteroids in amounts that are comparable to those seen in healthy controls (open circles).

Table III

FASTING LEVELS OF SERUM CORTICOIDS IN MUSCULAR DYSTROPHY (method of Klein et al (20))

Patient Age - Sex	Date	gamma %
D.H. 7 F	10/11/54 3/21/55	7.3 1.9
L.K. 14 M	2/12/55	10.0
B.H. 11 F	5/24/54 10/11/54	14.6 5.1
E.S. 6 M	11/10/52 2/27/54 4/8/55	5.3 4.4 8.3
P.D. 6 M	5/7/53	6.8
N.P. 6 M	10/18/54	7.5
G.Z. 9 M	1/16/53 3/31/55	27.1 27.5
W.S. 15 M	2/27/54 6/26/54 4/1/55	5.0 3.0 4.0
G.T. 13 M	3/14/55	8.9
K.S. 12 F	3/21/55	7.1
E.S. 10 M	3/11/55	0
T.W. 10 M	3/7/55	21.8
G.W. 7 M	3/14/55	3.4
D.E. 9 M	4/1/55	0
D.M. 15 M	4/1/55	13.3
H.S. 10 M	4/1/55	6.3
J.O. 11 M	4/11/55	0.6

Table IV

FASTING LEVELS OF SUGAR* IN VENOUS BLOOD OF CHILDREN WITH AND WITHOUT MUSCULAR DYSTROPHY

Group	Number	Mean ± S.D.	"p"
Muscular Dystrophy	70	84.3 ± 15.1	0.81
Control	68	85.4 ± 9.7	–

* Hagedorn-Jensen

oxysteroid excretion,[18] fasting blood levels of eosinophiles,[19] and concentrations of serum corticoids [20] were not remarkable. Only the serum corticoid data are shown in Table III.† The responses to water loads and to corticotropin (ACTH) (eosinophiles and 17-ketosteroids) were not unusual in the isolated patients in whom these observations were made.[21]

† Dr. Robert Klein and James Fortunato made these analyses.

Development of external genitalia and secondary sex characteristics appeared normal upon questioning and examination.

E. Carbohydrate Metabolism. — Fasting levels of venous blood sugar were not discernibly different from those recorded in a series of normal children under comparable conditions (Table IV).

Oral glucose tolerance tests, 1.75 gm. per kilogram of body weight with capillary blood sugars, showed no impairment of carbohydrate disposal (Fig. 4). This was also true of the intravenous dextrose tolerance tests at two levels of dosage with venous blood sugar measurements (Figs. 5 and 6).

The results of insulin tolerance tests (0.1 unit of crystalline insulin per kilogram of body weight with capillary sugar levels) in muscular dystrophy and in healthy controls are shown in Figure 7. In muscular dystrophy the drop in blood sugar is less than in normals, averaging 18.1±14.2 mg. per 100 cc. in the former, in contrast to 27.9±10.6 in the latter, with a *P*-value of 0.01.

COMMENT

The studies presented have resulted in the finding that serum protein-bound iodine levels are higher in children ill with muscular dystrophy than in healthy controls, though in most cases they remain within the range of normal. This presumably reflects a dynamic steady state of protein-bound-iodine metabolism which differs from that present in healthy children. At least three variables might be involved in producing the higher protein-bound iodine levels: (*a*) increased production and release by the thyroid gland, (*b*) increased binding by the serum proteins, and (*c*) decreased peripheral disposal via utilization in muscles and other tissues and degradation or excretion via the liver and gastrointestinal tract.[15] Only one definite comment based on our own studies is possible at this time concerning the contribution of these factors: The thyroxin tolerance tests suggest that peripheral disposal mechanisms are operating at rates comparable to those seen in health even

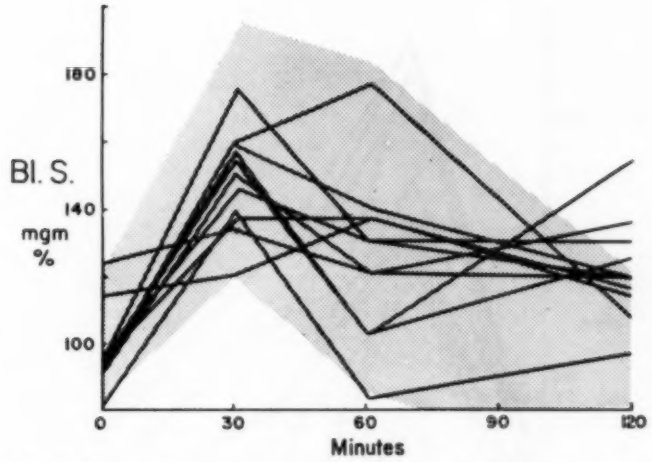


Fig. 4.—Oral glucose tolerance test in muscular dystrophy. The average capillary blood sugar concentrations ±2 S. D. prior to and following 1.75 gm. of glucose in 30 healthy boys and girls in a home for children is indicated by the dotted background. Children with muscular dystrophy showed a comparable rise and fall in blood sugar following the same dosage of glucose.

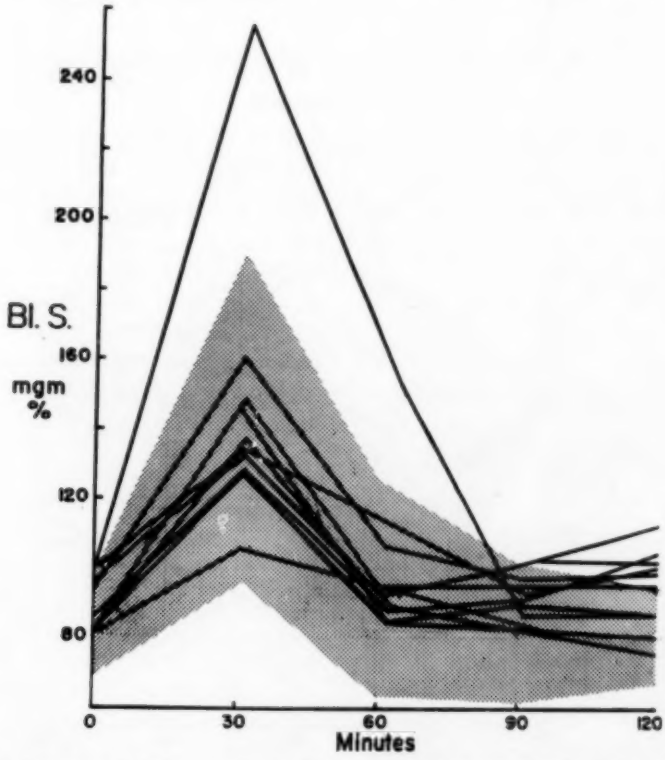


Fig. 5.—Response to intravenous dextrose. As in the oral glucose tolerance tests, the changes in serum blood sugar in children with muscular dystrophy, following 0.5 gm. of dextrose per kilogram I. V., indicated by solid lines, were of the same order of magnitude as that seen in 27 healthy children. The mean values ±2 S. D. for the latter group are indicated by the dotted background. The slight differences are not statistically significant. No explanation is available for the marked 30- and 60-minute rise in one of the patients with muscular dystrophy.

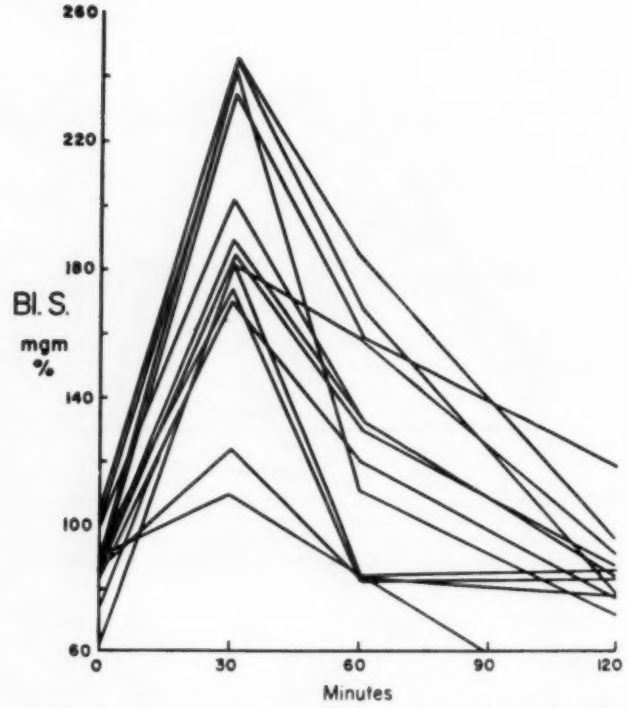


Fig. 6.—Blood sugar prior to and following the intravenous administration of dextrose. The injection of dextrose intravenously in larger dosage, 1.0 gm. per kilogram of body weight, resulted in rises in venous blood-sugar levels at 30 and 60 minutes which were greater than that seen during the 0.5 gm. per kilogram tolerances; however, the return to pretreatment values at 120 minutes points to an unimpaired ability to dispose of exogenous carbohydrate.

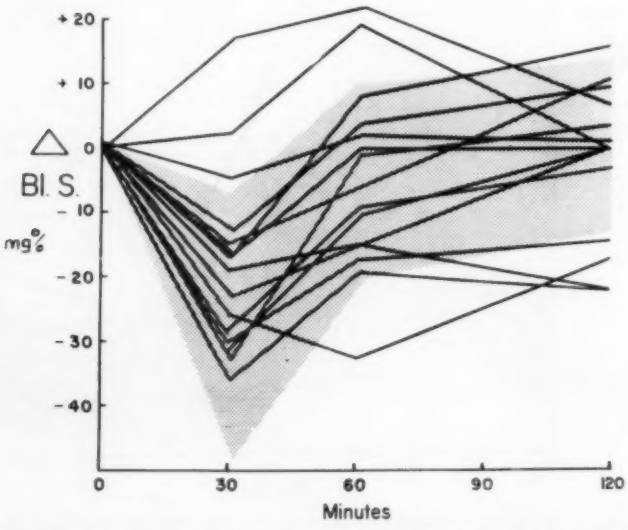


Fig. 7.—Changes in capillary blood sugar (milligram/100 cc.) following the intravenous injection of insulin in muscular dystrophy and in healthy controls. Crystalline insulin, 0.1 unit per kilogram of body weight, was injected intravenously at zero time. Capillary blood sugar values were obtained prior to this and at the 30-, 60-, and 120-minute points. The dotted background indicates the mean response ±2 S. D. in a group of 32 healthy children. It is evident by inspection and by calculation of the mean change that in muscular dystrophy the blood sugar decrease at 30 minutes is less than in healthy children (—18.1 ±14.2 in 15 children with muscular dystrophy versus —27.9 ±10.6 in 32 control studies).

though the muscle mass is not normal. On the other hand, it should be pointed out that circulating thyroxin which makes up all or almost all of the serum protein-bound iodine appears to be attached to the α-globulin fraction [22] and that studies in human and experimental muscular dystrophy have shown alterations in α- and β-globulin values.‡

Our patients showed numerous abnormal B. M. R. readings, both high and low. Others have reported elevated, normal, or depressed B. M. R. levels.§ These variations in B. M. R. values could reflect the non-applicability of ordinary surface-area tables to these children, some of whom have marked deformities of the body or the changes in muscle-mass : bone-fat ratios resulting from the disease process.

The somewhat elevated serum levels of calcium and of phosphorus do not fall into any recognized pattern of parathyroid or other endocrine disturbance.

The disposal of exogenous carbohydrate given per os or intravenously was normal. Previous reports have been at variance with one another indicating accelerated, diminished, or normal responses.‖ There is no evidence in our studies to support the sporadic impression ¶ that hypoglycemia is a feature of muscular dystrophy. This is in keeping with the conclusions of others.#

On the other hand, the muscular dystrophy children did show a smaller response to intravenous insulin. This suggests that with decrease in the muscle mass or with involvement by disease glycolysis is not accelerated to as great a degree under the impetus of insulin.

The serum protein-bound iodine levels are often higher in muscular dystrophy than in normals. The normal rate of disposal of exogenous thyroxin suggests that this steady state change is attributable either to increased thyroid hormone production and release or an increased binding capacity of serum proteins.

Responses in oral and intravenous glucose tolerance tests were within the ranges observed in healthy control subjects.

The capillary blood sugar change following intravenous insulin is less in muscular dystrophy than in normals; this represents a decreased acceleration of glucose metabolism in response to insulin and presumably reflects diminution in muscle mass or involvement by disease.

SUMMARY AND CONCLUSIONS

Measurements of serum corticoids and of urinary gonadotropin and 17-ketosteroid excretion reveal no pattern of abnormalities in children with muscular dystrophy.

‡ References 23 and 24.

§ References 7, 23, 25, and 26.

‖ References 7, 23, 26, 27, and 28-33.

¶ References 28, 31, and 33.

References 7, 23, 27, 34, and 35.

REFERENCES

1. Fetterman, G. H.; Wratney, M. J.; Donaldson, J. S., and Danowski, T. S.: Muscular Dystrophy: I. History, Clinical Status, Muscle Strength, and Biopsy Findings, A. M. A. J. Dis. Child., this issue, p. 326.

2. Girdany, B., and Danowski, T. S.: Muscular Dystrophy: II. Radiologic Findings in Relation to Severity of Disease, A. M. A. J. Dis. Child., this issue, p. 339.

3. Danowski, T. S.; Wirth, P. M.; Leinberger, M. H.; Randall, L. A., and Peters, J. H.: Muscular Dystrophy: III. Serum and Blood Solutes and other Laboratory Indices, A. M. A. J. Dis. Child., this issue, p. 346.

4. Danowski, T. S.: Electrolyte and Endocrine Studies in Muscular Dystrophy, Am. J. Phys. Med. **34**:281-285 (Feb.) 1955.

5. Gorbman, A.: Ultrafiltration of Urine for Collection and Biological Assay of Excreted Hypophyseal Hormones, Endocrinology **37**:177-190 (Sept.) 1945.

6. Talbot, N. B.; Sobel, E. H.; McArthur, J. W., and Crawford, J. D.: Functional Endocrinology from Birth Through Adolescence, Cambridge, Mass., Harvard University Press, 1952.

7. Shank, R. E.; Gilder, H., and Hoagland, C. L.: Studies on Diseases of Muscle: I. Progressive Muscular Dystrophy; A Clinical Review of 40 Cases, Arch. Neurol. & Psychiat. **52**:431-442 (Dec.) 1944.

8. Tyler, F. H., and Stephens, F. E.: Studies in Disorders of Muscle: IV. The Clinical Manifestations and Inheritance of Childhood Progressive Muscular Dystrophy, Ann. Int. Med. **35**:169-185 (July) 1951; Correction **35**:1164 (Nov.) 1951.

9. Nothacker, W. G., and Netsky, M. G.: Myocardial Lesions in Progressive Muscular Dystrophy, Arch. Path. **50**:578-590 (Nov.) 1950.

10. Zatuchni, J.; Aegerter, E. E.; Molthan, L., and Shuman, C. R.: The Heart in Progressive Muscular Dystrophy, Circulation **3**:846-853 (June) 1951.

11. Rubin, I. L., and Buchberg, A. S.: The Heart in Progressive Muscular Dystrophy, Am. Heart J. **43**:161-169 (Feb.) 1952.

12. Weisenfeld, S., and Messinger, W. J.: Cardiac Involvement in Progressive Muscular Dystrophy, Am. Heart J. **43**:170-187 (Feb.) 1952.

13. Sandberg, A. A.; Hecht, H. H., and Tyler, F. H.: The Heart in Muscular Dystrophy, Am. J. Med. **13**:498-499 (Oct.) 1952.

14. Danowski, T. S.: Interrelations of Thyroid and Iodine Metabolism, Maryland M. J. **2**:530-537 (Oct.) 1953.

15. Danowski, T. S.; Schwartz, R.; Rhodes, G. J.; Yoder, R. D.; Puntereri, A. J., and Mateer, F. M.: Serum Protein-bound Iodine Levels Following Administration of Thyroxin in Various Diseases, J. Clin. Endocrinol. **15**:1116-1130 (Sept.) 1955.

16. Venning, E. H., and Kazmin, V.: Excretion of Urinary Corticoids and 17-Ketosteroids in the Normal Individual, Endocrinology **39**:131-139 (Aug.) 1946.

17. Holtorff, A. F., and Koch, F. C.: Colorimetric Estimation of 17-Ketosteroids and Their Application to Urine Extracts, J. Biol. Chem. **135**: 377-392 (Sept.) 1940.

18. Glenn, E. M., and Nelson, D. H.: Chemical Method for the Determination of 17-Hydroxycorticosteroids and 17-Ketosteroids in Urine Following Hydrolysis with β-Glucuronidase, J. Clin. Endocrinol. **13**:911-921 (Aug.) 1953.

19. Forsham, P. H.; Thorn, G. W.; Prunty, F. T. G., and Hills, A. G.: Clinical Studies with Pituitary Adrenocorticotropin, J. Clin. Endocrinol. **8**:15-66 (Jan.) 1948.

20. Klein, R.; Papadatos, C.; Fortunato, J., and Byers, C.: Acid-Hydrolyzable Corticoids of Serum, J. Clin. Endocrinol. **15**:215-226 (Feb.) 1955.

21. Soffer, L. J., and Gabrilove, J. L.: A Simplified Water-Loading Test for the Diagnosis of Addison's Disease, Metabolism **1**:504-510 (Nov.) 1952.

22. Albright, E. C.; Larson, F. C., and Deiss, W. P.: Thyroxine Binding Capacity of Serum Alpha Globulin in Hypothyroid, Euthyroid, and Hyperthyroid Subjects, J. Clin. Invest. **34**:44-47 (Jan.) 1955.

23. Tyler, F. H., and Perkoff, G. T.: Studies in Disorders of Muscle: VI. Is Progressive Muscular Dystrophy an Endocrine or Metabolic Disorder? A. M. A. Arch. Int. Med. **88**:175-190 (Aug.) 1951.

24. Oppenheimer, H.; Milman, A. E., and Milhorat, A. T.: Electrophoretic Studies of Nutritional Muscular Dystrophy in Rabbits, Fed. Proc. **14**:109 (March) 1955.

25. Garot, L.: Contribution à l'etude des troubles du métabolisme chimique dans la dénutrition grave du nourrisson: III. Excrétion créatinque et métabolisme basal, Rev. franç. pédiat. **9**:273-312, 1933.

26. Guarnaschelli-Raggio, A.: La proteinemia nella distrofia muscolare progressiva primitiva, Arch stud. fisiopat. **6**:391-398 (Sept.-Oct.) 1938.

27. Hurwitz, S.: Primary Myopathies: Report of 36 Cases and Review of the Literature, Arch. Neurol. & Psychiat. **36**:1294-1316 (Dec.) 1936.

28. Janney, N. W.; Goodhart, S. P., and Isaacson, V. I.: The Endocrine Origin of Muscular Dystrophy, Arch. Int. Med. **21**:188-215 (Feb.) 1918.

29. Magee, M. C.: Creatine and Creatinine Metabolism in Progressive Muscular Dystrophy: Report of 2 Cases and Controls, Am. J. Dis. Child. **43**:19-31 (Jan.) 1932.

30. Van Bekkum, D. W., and Querido, A.: Inorganic Phosphate Response to Intravenous Glucose Administration in Progressive Muscular Dystrophy, J. Clin. Invest. **32**:1061-1064 (Nov.) 1953.

31. McCrudden, R. H., and Sargent, C. S.: Hypoglycemia and Progressive Muscular Dystrophy, Arch. Int. Med. **17**:465-475 (April) 1916.

32. Gibson, R. B.; Martin, F. T., and Van Rennselaer, Buell, M.: A Metabolic Study of Progressive Pseudohypertrophic Muscular Dystrophy and Other Muscular Atrophies, Arch. Int. Med. **29**: 82-96 (Jan.) 1922.

33. Byard, D. S.: Muscular Dystrophy, Internat. Clin. **1**:174-177, 1923.

34. Bramwell, E.: Muscular Dystrophy, Sympathetic System and Endocrine Glands, Lancet **2**: 1103-1109 (Nov. 28) 1925.

35. Hughes, T. A., and Shrivastata, D. L.: Carbohydrate Tolerance in Two Cases of Muscular Dystrophy, Indian J. M. Res. **15**:437-443 (Oct.) 1927.

Adrenal Pheochromocytoma Simulating Diabetes Insipidus

Report of a Case and Review of the Other Pediatric Cases

FETHI TEVETOĞLU, M.D.
and
CHI-HAO LEE, M.D., Corpus Christi, Texas

Hypertension is an unusual finding in children, and it is almost always the manifestation of some serious underlying disease process. The majority of cases are secondary to renal diseases of various nature, such as acute and chronic glomerulonephritis, pyelonephritis, nephrosis, polycystic kidney, hypoplastic kidney, hydronephrosis, cyst and tumor, renal tuberculosis, aneurysm of renal artery, amyloid kidney, periarteritis nodosa, lower nephron nephrosis, Goldblatt syndrome, and uremia. Even conditions outside but adjacent to the kidney, like perinephritis or a retroperitoneal mass causing pressure on the kidney, will at times cause high blood pressure.

Other important causes of hypertension can be grouped roughly into the following categories for the purpose of diagnostic workup: I. Cardiovascular: coarctation of aorta, patent ductus arteriosus, aortic insufficiency, mitral stenosis, arteriosclerosis, and polycythemia (Gaisböck). II. Central nervous system: increased intracranial pressure, encephalitis, poliomyelitis, and hypothalamic tumor. III. Endocrine: Cushing's syndrome, hyperthyroidism, diabetes mellitus, pheochromocytoma, and therapy with corticotropin and cortical hormones. IV. Poisoning: chronic lead poisoning, acrodynia, thallium, vitamin D, epinephrine, black widow spider, and carbon monoxide. V. Miscellaneous: Newborn infant of eclamptic mother, high sodium and chloride intake, familial autonomic dysfunction (Riley-Day), rheumatic fever, scarlet fever, diphtheria, obesity, anxiety, porphyria, and a few cases of so-called "essential" or "idiopathic" hypertension.

The treatment of many of these conditions is often unsatisfactory; therefore the early diagnosis of one small group, namely, pheochromocytoma, in which surgical intervention may effect an immediate relief of a progressive and fatal hypertension, is highly important. These are the cases of paroxysmal or sustained hypertension due to pheochromocytoma or paraganglioma tumors of chromaffin tissue originating from mature pheochromocytes. These tumors produce at least two active substances, epinephrine and arterenol, and are capable of becoming malignant and metastasizing.

Although the number of cases of pheochromocytoma reported among adults is rapidly increasing, the disorder is still a rarity in the pediatric age group. Recently we have diagnosed such a case in an 8-year-old boy and have successfully removed the tumor. This case is especially interesting in that it had been diagnosed and treated as a case of diabetes insipidus for 18 months before the patient was referred to us. While reviewing the literature, we have noticed that, although not uniformly present, polyuria and polydipsia were prominent symptoms in several cases in children. We are presenting our case and at the same time reviewing 47 cases of pheochromocytoma previously reported in children under 16 years of age.

Received for publication Sept. 27, 1955.
From Driscoll Foundation Children's Hospital.

REPORT OF CASE

An 8-year-old white boy was admitted to the Driscoll Foundation Children's Hospital on Sept. 9, 1954, with the chief complaints of excessive intake of liquids and increased urinary output of 18 months' duration.

He had been in apparent good health until two years previously, at which time upper respiratory infections became frequent. Eighteen months prior to admission he had measles, following which polydipsia and polyuria were noted. His daily fluid intake was in the range of 5 to 7 liters, and urination increased both in frequency and volume, with nocturnal enuresis. A diagnosis of diabetes insipidus was made. Administration of 1 cc. of vasopressin (Pitressin) every two or three days resulted in a decrease in the amount of polyuria and polydipsia.

From the onset of illness the patient also developed excessive sweating, headache, nervousness, palpitation, weakness, poor weight gain, intermittent muscle and joint pains, marked anxiety, visual disturbances in the form of spots and stars, and a low-grade fever, the temperature varying between 99 and 102 F. An excretory urogram, one month before admission, was reported negative. Concentration tests disclosed an inability to concentrate urine beyond a specific gravity of 1.005. A small amount of albumin had been present in all the urinary specimens. The tentative diagnosis was chronic glomerulonephritis. Vasopressin therapy was continued, and a salt-free diet was instituted, without much change in the symptoms.

The child had been delivered by Caesarean section; otherwise, the past history was uneventful. The family history was not contributory.

Physical examination on admission revealed a thin, pale, alert, and anxious-looking child. His weight was 46 lb.; his height, 50¾ in. Temperature was 99.8 F. Slightly enlarged lymph nodes were present in the cervical, axillary, and inguinal regions. The hands and feet were cold and clammy. The tonsils were hypertrophic. Strong pulsations were visible in the neck. Heart rate was 120 per minute, and the rhythm was regular. The apical impulse was forceful and was palpated in the sixth intercostal space, about 1 cm. outside of the left nipple line. The heart sounds were loud. A Grade 2 systolic murmur was heard at the apex and was transmitted to the axilla and left sternal border. The blood pressure was 180/136 mm. Hg in the left arm and 180/128 in the right arm, 194/144 in the left leg, and 190/140 in the right leg. The abdomen was free of palpable masses; the liver and spleen were not enlarged. External genitalia were normal. The ocular fundi showed evidences of papilledema in the left eye and of subsiding papilledema in the right eye. Following admission the patient was very tempermental in disposition, with frequent "temper tantrums."

Laboratory Data.—The initial examination of the urine showed a specific gravity of 1.005, with a slight trace of albumin; Addis count was within normal range. Hemogram and sedimentation rate were normal. Test for C-reactive protein was negative. VDRL test was negative. Urea clearance showed $C_{max.}$=89.5 cc. blood cleared per minute. Nonprotein nitrogen was 46 mg/100 ml. blood. Serum chloride was 95 mEq/liter; potassium was 5 mEq/liter; sodium, 139 mEq/liter; cholesterol, 268 mg/100 ml.; creatinine, 0.7 mg/100 ml.; urea N, 16 mg/100 ml.; fasting blood sugar, 93 mg/100 ml.; uric acid, 2.5 mg/100 ml.; calcium, 10.4 mg/100 ml.; phosphorus (inorg.), 4.3 mg/100 ml.; CO_2-combining power, 24.7 mEq/liter; PBI, 4.4 γ/100 ml.; total protein, 6.1 gm/100 ml.; albumin, 3.9 gm/100 ml., and A/G ratio 1.8. Glucose-tolerance test: fasting blood sugar, 106 mg/100 ml.; 30 minutes, 202 mg.; 1 hour, 183 mg., and 2 hours, 60 mg. Basal metabolic rate was +22%. The electrocardiogram showed evidences of possible myocardial damage and left axis deviation. Roentgenograms of the thorax, skull, abdomen, and excretory urography revealed no abnormality.

Special Tests of Adrenalytic Drugs: On Sept. 25, 1954, an intravenous piperoxan test was done. The child was allowed to rest about one-half hour in a supine position, until the blood pressure was stabilized. An intravenous drip of isotonic saline was started, and blood pressure readings were taken at one-minute intervals. Piperoxane hydrochloride, 9 mg. was injected over a period of two minutes. A sharp fall in blood pressure, from 190/140 to 140/90 mm. Hg, occurred within 2 minutes, followed by gradual rise to initial level in 20 minutes.

On Sept. 26, 1954, phentolamine (Regitine) hydrochloride, 25 mg., was given orally as the test dose; a very satisfactory fall in blood pressure, from 160/110 to 114/88 mm. Hg, occurred within 65 minutes and persisted for about 3½ hours.

On Sept. 29, 1954, intravenous injection of 1 mg. of phentolamine hydrochloride resulted in an immediate sharp fall of blood pressure, from 210/140 to 140/80 mm. of Hg, which gradually returned to 178/130 mm. Hg within 22 minutes (Fig. 1).

Hospital Course.—After admission the patient was put on a regular diet. Fluid intake and urinary output ranged from 4 to 7 liters in 24 hours, and urinary specific gravity was constantly below 1.006. Blood pressure was constantly elevated, from a high of 210/140 to a low of 160/120 mm. Hg. The patient was put on phentolamine hydrochloride therapy orally, from Sept. 30 until Nov. 16 (total, 48 days) in increasing dosage: 25 mg. every 4 hours for 11 days, 37.5 mg. every 4 hours for 28 days, and 50 mg. every 4 hours for 9 days. A moderate fall

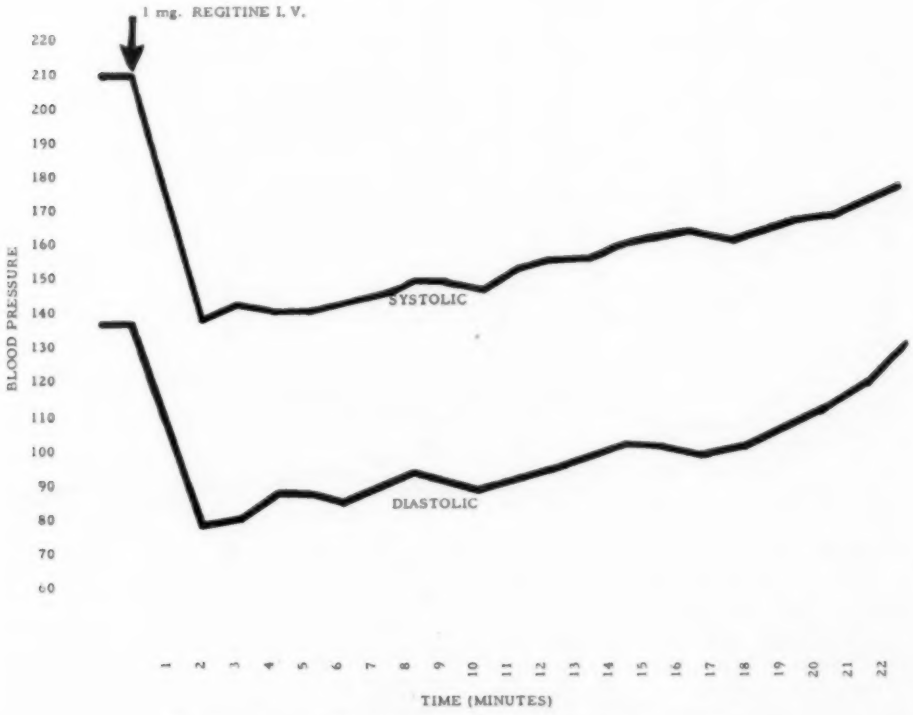


Fig. 1.—Response of the blood pressure to intravenous phentolamine.

in blood pressure with some fluctuation was observed, which during the week of Nov. 9 to Nov. 16 varied from a high of 170/120 to a low of 138/98 mm. Hg. During the 48 days of phentolamine treatment, fluid intake and output showed about 50% drop, and the patient gained 6 lb.; his cardiologic and ophthalmologic signs were unchanged. He was still at times belligerent and uncooperative to the point of being maniacal. He bit and kicked the nurses a few times during the administration of injections, or other painful procedures. However, his crying was usually unproductive of tears.

Retroperitoneal Pneumography.—Retroperitoneal pneumography was performed by injecting 800 cc. of air into the areolar tissue of the presacral area. The roentgenologic findings suggested the presence of a mass in the right adrenal region.

Operation.—On Nov. 16, 1954, the patient was prepared for surgery with 5 mg. phentolamine hydrochloride given as intravenous drip in 250 cc. of 2.5% dextrose in half-isotonic saline solution. After premedication with meperidine (Demerol) hydrochloride, 50 mg., and atropine, 1/200 grain (0.3 mg.), thiopental (Pentothal) sodium solution, 0.4% with 0.5 cc. curare was administered, and anesthesia was continued with nitrous oxide, ether, and oxygen. A complete upper abdominal transverse incision was made, beginning at the ninth interspace on the left and extending to the ninth interspace on the right. Both rectus muscles were transected. At this point, before the peritoneum had been entered, the child suddenly had a convulsion, which lasted approximately 45 seconds. The operation was interrupted for approximately 10 minutes. The abdomen was entered, and complete exploration revealed a tumor in the right adrenal gland. A longitudinal incision was then made in the peritoneum of the right gutter; the duodenum was drawn medialward and downward; the kidney was drawn downward, and the adrenal gland on the right was exposed. Care was taken not to manipulate or palpate the tumor more than necessary. As the artery and vein from the inferior phrenic were ligated, the blood pressure dropped to approximately 100/80 mm. Hg (Fig. 2). The patient remained in good condition, and the blood pressure never dropped below 90 mm. Hg systolic. The well-encapsulated tumor was removed. A small portion of normal adrenal gland, consisting of 1 or 2 gm. of tissue, was left at the apex. After removal of the tumor, methoxamine

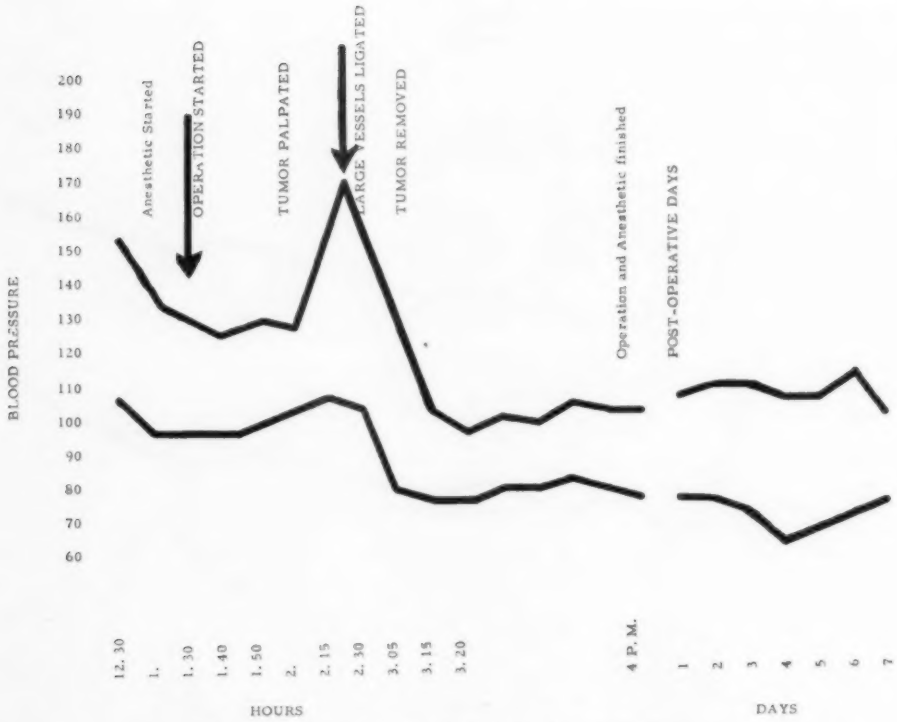


Fig. 2.—Blood pressure during and following the operation.

(Vasoxyl) hydrochloride, 0.5 cc., was administered. No epinephrine, arterenol, or phentolamine was needed, although they were readily available. The wound was closed without drainage.

Pathology of the Tumor.—Gross Examination: The growth was a firm faintly yellowish-gray completely encapsulated tumor, weighing 9 gm. and measuring 3.5 by 2.5 by 2 cm. On section the cut surface was firm, yellowish-gray, and finely granular and showed scattered small foci of hemorrhage. The neoplasm merged inseparably with the adrenal medulla, and at one pole a narrow zone of yellowish adrenal cortex was evident.

Microscopic Examination: The tumor merges inseparably with the medulla of the adrenal. The neoplasm shows an alveolar and pseudoalveolar configuration consisting of medium and large polymorphous epithelial-like cells that show a granular and vacuolated cytoplasm. Their nuclei are pleomorphic and markedly hyperchromatic. Single and multinucleated tumor giant cells and syncytial formations are present. The alveoli are supported in a delicate fibrocapillary stroma, and the neoplasm is traversed by large sinusoidal blood spaces. Foci of thrombovascular necrosis are present. This is regarded as a benign tumor. Diagnosis: Adrenal gland pheochromocytoma.

Postoperative Course.—Postoperatively, the patient was afebrile. His blood pressure stayed around 110/70 mm. Hg (Fig. 2). Fluid intake and urinary output were normal. Urinary specific gravity increased to 1.015. He no longer sweated excessively, and he had no headaches or muscle and joint pains. Intravenous phentolamine and piperoxan tests were repeated 16 and 17 days after operation, respectively; both gave negative results. Basal metabolic rate was —5% on the 14th postoperative day. Heart sounds were normal, without murmurs. The electrocardiogram was reported normal. Eye examination showed subsiding papilledema. The peripheral vasomotor phenomena, such as coldness and duskiness of hands and feet and pallor of the face, improved. The patient was discharged 18 days after operation. When last seen, on July 1, 1955, six months after discharge, he was in very good condition. At that time his blood pressure was 100/65 mm. Hg. There had been no polyuria, polydipsia, nocturia, or enuresis postoperatively. The child's behavior was considerably improved. He had gained 13 lb. since discharge.

REVIEW OF THE LITERATURE

In 1886 Fränkel [22] reported finding bilateral adrenal tumors at the autopsy of an 18-year-old girl. In 1892 Berdez [4] reported and described a vascular encapsulated tumor within the medulla of the right adrenal gland. Manasse,[47] in 1893, reported a tumor which showed the characteristics of a pheochromocytoma. Three years later, he reported a second case in which he demonstrated the chromaffinity of the cells composing the tumor.[48] Marchetti,[50] in 1904, described a bilateral pheochromocytoma of the adrenal medulla, occurring in a 15-year-old boy. This is also the first pediatric case report. Suzucki,* in 1909 and 1910, reported three cases in adults, one of which was necrotic and cystic. Wiesel [77] and Neusser,[55] in 1909 and 1910, reported the unusual occurrence of this tumor in a 2-year-old girl, who had the vascular changes of an epinephrine sclerosis, cerebral arteriosclerosis, and at the same time they included a case of Kolisko's, the first in which signs of vasomotor instability were noted. Pick,[56] in 1912, suggested the advisability of naming the tumor from the predominating type of cell—in this case the pheochromocyte—the name of which, originated by Poll,[58] is generally accepted. In 1913 Helly [30] reported a case with hypertension and glycosuria without renal or pancreatic disease. Harbitz,[29] in 1915, reported a chromaffin-cell tumor of the adrenal as occurring in conjunction with a hypernephroma. The characteristic clinical picture, with paroxysmal hypertension, was described for the first time in 1922 by L'Abbe, Tinel, and Doumer,[39] and the clinical diagnosis was first established by Vaquez and Donzelot,[73] in 1926. The first tumor of this nature to be removed at operation was the case of Masson and Martin,[51] in 1923. The first case in which the diagnosis was made prior to operation was that of Pincoffs,[57] in 1929. This tumor was removed surgically by Shipley.[63] In the last 30 years, cases of pheochromocytoma have been reported with increasing frequency (Table 1).

TABLE 1.—*Review of Cases of Pheochromocytoma by Various Authors*

Author	Year	Cases Collected, No.
Wahl [74]	1914	13
Biebl & Wichels [7]	1925	14
Rabin [60]	1929	25
Eisenberg & Wallerstein [17]	1932	53
Belt & Powell [3]	1934	60
MacKenzie & McEachern [46]	1938	82
Brunschwig & Humphreys [12]	1939	103
Kirschbaum & Balkin [34]	1942	116
MacKeith [45]	1944	165
Goldenberg, Snyder, & Aranow [24]	1947	134
Calkins & Howard [14]	1947	176
Smithwick, Greer, Robertson, & Wilkins [66]	1950	270
Davis, Hull, & Vardell [16]	1950	208
Graham [27]	1951	207

The first review of the cases occurring in children was published by Snyder and Vick,[68] in 1947. Litman and State,[42] in 1949, added a case of their own to the seven cases summarized by Snyder and Vick. Goldfarb [25] mentioned in his article, in 1953, a total of 15 cases occurring in children under 14 years of age; however, 2 of the 15 cases were reported and counted twice. In April, 1954, Negri and Vanoni,[53] tabulated 15 cases of pheochromocytoma in children under 14 years of age and reported a case of their own. In August, 1954, Daeschner and co-workers [15] analyzed the clinical courses of 17 cases of proved pheochromocytoma in children under 14 years of age, but they did not list the individual cases. In July, 1955, Smid and DuShane [65] reported 1 case and also listed 27 other pediatric cases.

Stimulated by the interest in our own case, we were able to discover 47 other cases of proved pheochromocytoma in children 16 years or under reported in world literature (Table 2).

SUMMARIES OF REPORTS OF PEDIATRIC CASES †

CASE 1 (Marchetti,[50] 1904).—A white boy, aged 15 years, who died of typhoid, was found at necropsy to have bilateral pheochromocytoma of the adrenal medulla.

CASE 2 (Wiesel,[77] 1909).—A white girl, aged 2 years, who died of bronchopneumonia, was found at necropsy to have a pheochromocytoma and the vas-

* References 70 and 71.

† Duplications of cases reported are noted.

TABLE 2.—*Reported Cases of Pheochromocytoma in Children*

Case No.	Author	Age, Yr.	Sex	Race*	Site of Tumor	Diagnosis†	Operation	Result‡
1	Marchetti [80] (1904)	15	M	W	Both adrenals	N	No	..
2	Wiesel [77] (1909)	2	F	W	.....	N	No	..
3	Wahl [74] (1914)	2½	F	W	L. adrenal with metastases	N	No	..
4	Kremer [88] (1936)	14	F	..	Both adrenals	N	No	..
5	Evans [19] (1937)	12	F	W	L. adrenal	N	No	..
6	Neff [83] (1942)	1 4/12	F	W	L. adrenal	O	Yes	L
7	Linde [40] (1942)	5/12	M	..	R. adrenal	O	Yes	L
8	Linneweh [41] (1942)	10	M	W	Both adrenals	O	Yes	D
9	Evans & Stewart [20] (1942)	14	F	N	R. adrenal	..	Yes	L
10	Gørtz [30] (1945)	10	M	W	L. adrenal with metastases	C	Yes	D
11	Snyder & Vick [69] (1947)	11	M	W	R. adrenal	C	Yes	D
12	Snyder & Vick [68] (1947)	12	F	W	L. adrenal	C	Yes	L
13	Snyder & Vick [68] (1947)	11	F	N	Bifurcation of aorta Foramen of Winslow	C	Yes	D
14	Goldenberg [24] (1947)	12	M	..	R. adrenal	C	Yes	L
15	Brewer [10] (1949)	..	..	..	.....	..	....	..
16	Grimson [28] (1949)	10	M	N	R. adrenal	C	Yes	L
17	Litman & State [42] (1949)	11	F	..	R. adrenal	C	Yes	D
18	Seelemann [64] (1950)	13	F	W	Both adrenals	C	Yes	D
19	Koffler [37] (1950)	12	M	N	R. adrenal	C	Yes	L
20	McCoy & Bridgeman [44] (1950)	13	F	W	L. adrenal	C	Yes	L
21	Brachetto-Brian & Brewer [9] (1950)	13	M	..	.....	..	....	..
22	Hubble [31] (1951)	11½	M	W	Both adrenals and anterior to aorta	C	Yes	D
23	Berkheiser & Rappoport [6] (1951)	11	F	W	L. adrenal	N	No	..
24	Bastrup-Madsen [2] (1951)	9	F	..	L. adrenal	N	No	..
25	Faber [21] (1951)	13	F	..	.....	C	Yes	..
26	Iseri [32] (1951)	8	M	N	Below l. kidney	C	Yes	..
27	Apter [1] (1951)	14	F	W	R. adrenal	C	Yes	L
28	Soffer [69] (1951)	7	M	..	.....	..	....	..
29	Neill & Smith [54] (1952)	6	M	..	Both adrenals	N	No	..
30	Talbot [73] (1952)	6	M	..	Both adrenals	..	Yes	D
31	Klein [35] (1953)	11	M	..	.....	..	....	..
32	Goldfarb [25] (1953)	9	M	N	Both adrenals	N	No	..
33	Berg [5] (1953)	15	M	..	Both adrenals	N	Yes	D
34	Wen & Fu [76] (1953)	14	M	Ch	R. adrenal	C	No	..
35	Schaefer & Christopher [61] (1954)	10	M	W	Both adrenals	N	No	..
36	Israelski [33] (1954)	10	M	..	R. adrenal	C	Yes	L
37	Negri & Vanoni [58] (1954)	12	M	W	R. adrenal	C	Yes	L
38	Popper & Theron [59] (1954)	13	M	N	R. adrenal	..	Yes	L
39	Weiman [75] (1954)	14	F	W	Medial to r. kidney	C	Yes	D
40	Daeschner [15] (1954)	4	M	W	R. adrenal	C	Yes	L
41	Schleisner [62] (1954)	..	..	..	Both adrenals	..	....	..
42	Manger [49] (1954)	12	M	..	.....	C	Yes	L
43	Lukemeyer [43] (1954)	7	M	W	R. adrenal	C	Yes	L
44	Snyder & Rutledge [67] (1955)	13	M	W	R. adrenal	C	Yes	L
45	Smid & DuShane [65] (1955)	12	M	W	L. adrenal	C	Yes	L
46	Young & Murray [78] (1955)	15	M	..	.....	C	Yes	L
47	Young & Murray [78] (1955)	12	M	..	.....	N	No	..
48	Tevetoglu & Lee (1955)	8	M	W	R. adrenal	C	Yes	L

* W, white; N, Negro; Ch, Chinese.
† C, clinical evidence; N, necropsy; O, operation.
‡ L, living; D, dead.

cular changes of an epinephrine sclerosis. This case was also cited in Neusser and Wiesel's book.[55]

CASE 3 (Wahl,[74] 1914).—A white girl, aged 2½ years, had marked anemia for several months and fever, abdominal distention, and tenderness of three weeks' duration. Examination revealed a mass in the umbilical region and enlarged inguinal lymph nodes. A sister, who died a few years before, had a similar clinical course. Necropsy on the patient revealed a tumor in the left adrenal region and another at the root of the small mesentery. Metastatic tumors were present in the liver and kidney. Three different types of tumor cells (ganglioneuroma, chromaffin, and malignant neuroblastoma) were found histologically in the tumors.

CASE 4 (Kremer,[88] 1936).—A girl, aged 14 years, presented a picture of hypertension, cardiac hypertrophy, changes in the eyegrounds, and abnormal urinary findings. Hypertension was paroxysmal in the beginning, later became sustained. A necropsy

was performed after the girl died suddenly, and a medullary tumor was found in each adrenal gland. It was postulated that the symptoms were related to these tumors.

CASE 5 (V. L. Evans,[19] 1937).—A white girl, aged 12 years, had complained of paroxysms of palpitation, headache, excessive sweating, and polyphagia of four years' duration. Her blood pressure rose as high as 285/230. The eyegrounds showed papilledema, arterial spasm, and exudates. Her basal metabolic rate was +60%. She died during an attack, and at necropsy a tumor the size of a hen's egg was found behind the tail of the pancreas, attached to the left adrenal gland. Histologically this was pheochromocytoma.

CASE 6 (Neff,[52] 1942).—A white girl, aged 16 months, showed obesity; generalized hirsutism, particularly involving the pubic region; a bone age of over 2 years, and large adult-like genitalia. The systolic pressure ranged from 140 to 180. Pyelograms and perirenal aerograms showed a mass above the left kidney. Blood pressure rose gradually to 200 systolic, and the tumor became palpable. The hypertension was sustained. The tumor was removed. When seen a year after operation the infant showed a normal blood pressure and complete regression of the hirsutism and genital changes. The tumor had abundant chromaffin granules and no trace of adrenal cortical elements. The authors suggested a functional derangement of the adrenal cortex through the mechanical pressure of the underlying medullary tumor.

CASE 7 (Linde,[40] 1942).—A boy, aged 5 months, had attacks of sudden crying and drawing up of the legs as if in severe pain, of four months' duration. These attacks were also accompanied by sweating and vomiting, and occasionally by convulsions. During the course of the investigation a mass to the right of the upper pole of the right kidney was discovered on physical examination and confirmed by urogram. The tumor was removed surgically, and this resulted in subsidence of the symptoms. The tumor was identified histologically as malignant pheochromocytoma.

CASE 8 (Linneweh,[41] 1942).—A white boy, aged 10 years, who had been sick for a year with progressive weakness, loss of weight, visual disturbances, cold sweats, polydipsia, and polyuria, was found on examination to have a sustained high blood pressure. The eyegrounds showed severe albuminuric retinitis. Pyelogram showed pronounced hydronephrosis, with hydroureter on the left. The diagnosis of hypertension due to unilateral renal disease was made, and left nephrectomy was performed. During the operation a tumor of the left adrenal gland was seen, and this was removed at a later operation. Hypertension was not relieved, and the boy died in congestive heart failure six weeks later. At necropsy a second tumor was found, in the right adrenal gland. Both tumors were composed of chromaffin. Knake[30] described the pathological findings of this case in great detail in another report.

CASE 9 (W. F. Evans, and Stewart,[20] 1942).—A Negro girl, aged 14 years, was admitted with a chief complaint of blurring of vision of five months' duration. The patient first developed weakness and sweating three years prior to admission, which was followed by the appearance of dyspnea, polydipsia, polyuria, headache, and signs of vasomotor instability. On admission her blood pressure was 210/120. Examination also revealed marked eyeground changes and cardiomegaly with rough systolic murmur. The urine contained albumin, and the basal metabolic rate was +46%. Perirenal insufflation of CO_2 was carried out, and a mass with visible calcification in the region of the right adrenal gland was discovered on radiographs. Right adrenalectomy was performed, and the tumor removed was reported to be pheochromocytoma of low-grade malignancy. The patient was relieved of the symptoms and was doing well after the operation.

CASE 10 (Gørtz,[26] 1945).—A white boy, aged 10 years, had been ill for six months with the chief complaint of headache. He had sustained high blood pressure in the range of 210-265 systolic, accompanied by hypertensive retinopathy. Blood examination showed doubtful increase of epinephrine. Albumin was present in the urine. The patient also showed increased perspiration, and there was somnolence in the later stage. Adrenal tumor was suspected, and arbitrarily the left side was selected to be explored through a lumbar incision. The blood pressure dropped even before the adrenal was reached. No tumor was found, and the operation was terminated because of the poor condition of the patient. He died six hours later. At necropsy a tumor was found in front of the large vessels, connected by a pedicle with the lower mesial angle of the left adrenal gland—a location which would have been disclosed through an abdominal incision. Microscopically the tumor was reported to be a malignant pheochromocytoma which had invaded a vein.

This case was also reported by Espersen and Dahl-Iversen,[18] in 1946.

CASE 11 (Snyder and Vick,[68] 1947).—A white boy, aged 11 years, was admitted with the chief complaints of severe headache and sweating of two months' duration and disturbed vision for three days. The patient appeared tense and anxious on admission. The blood pressure was around 260/210 in all four extremities. There were eyeground changes accompanied by alterations of the visual fields. Restriction of fluid intake led to rise in temperature and blood pressure and great discomfort. One episode of sudden elevation of blood pressure to over 300 accompanied by maniacal behavior

was dramatically relieved by magnesium sulfate. Perirenal air injection revealed a mass in the right adrenal region. The tumor was removed through a right lumbar incision. The blood pressure fluctuated widely during the operation. It became unobtainable, and the patient died two and one-half hours after the operation. Chromaffin tissue was demonstrated in the tumor.

CASE 12 (Snyder and Vick,[68] 1947).—A white girl, aged 12 years, was admitted four times to the hospital before a diagnosis of pheochromocytoma was made. Her chief complaints were profuse sweating and loss of weight despite a good appetite, of two years' duration. Polydipsia and intolerance to hot weather were also presenting symptoms. Physical examination showed markedly elevated blood pressure in all four extremities, progressive papilledema and vascular changes in the eyegrounds, and a tense and anxious expression. BMR was elevated to over +50%. On x-ray examination a small calcified fleck was seen above the left kidney. Perirenal air injection revealed an enlarged left adrenal gland. A well-encapsulated tumor was removed at operation; however, the hypertension and other symptoms persisted. Blood from the patient injected into two cats caused drop of blood pressure and prompt death of the cats. On the basis of two positive piperoxan tests, another operation was performed transperitoneally. A second tumor was found medial to the left adrenal gland, just superior to the pancreas, and was removed. All abnormal symptoms subsided after the second operation. Both tumors were identified as pheochromocytoma pathologically.

This case was also described later by Goldenberg and co-workers,[24] Ganem and Cahill,[23] Cahill,[13] and Bruce.[11]

CASE 13 (Snyder and Vick,[68] 1947).— A Negro girl, aged 11 years, had been suffering from severe headache accompanied by vomiting and abdominal pain at times for several years. Her blood pressure was in the range of 180/136-230/145. Vascular changes in eyegrounds and left-sided cardiomegaly were also present. The BMR was markedly elevated (+48% to +67%). Piperoxan tests showed positive response, but perirenal insufflation of air revealed no abnormality. Exploratory laparotomy was performed through a transverse upper abdominal incision. Two tumors were found, one near the bifurcation of the aorta and the other filling the foramen of Winslow, both independent of the kidneys and of the adrenal glands. The patient died during the manipulation of the tumors, which were pheochromocytomas.

This case was also described by Goldenberg and co-workers,[24] Bruce,[11] and Cahill.[13]

CASE 14 (Goldenberg and co-workers,[24] 1947).— A boy, aged 12 years, was admitted to the hospital with the chief complaint of blurring of vision for one week. Papilledema, hemorrhages, and exudates were observed in the eyegrounds at the time of admission. For the previous two or three years the patient had also had attacks of excessive diaphoresis and thirst, headache, abdominal pain, nausea and vomiting, pallor, and palpitation, usually associated with excitement or emotional disturbance. Blood pressure was elevated to 260/190 in all extremities on admission, but later on it dropped to 118/82 spontaneously. During the paroxysm of hypertension, a piperoxan test was done and showed positive response. Studies with air injection disclosed a small right kidney. The patient was explored through an abdominal incision. The right kidney was hypoplastic, with a tumor attached. They were removed together. The tumor was reported to be pheochromocytoma. The abnormal symptoms and signs subsided.

This case was also reported in Bruce's [11] article.

CASE 15 (Brewer,[10] 1949).—This is the report of an infant with pheochromocytoma; the original article could not be obtained.

CASE 16 (Grimson and co-workers,[28] 1949).— A Negro boy, aged 10 years, presented a history of recurrent right-sided abdominal pain, fatigue, and dyspnea on exertion for about 10 months. His blood pressure ranged from 208/160 to 176/130 during the hospital stay. The paroxsyms of higher blood pressure were accompanied by sweating, headache, and tachycardia. Positive response was obtained with repeated piperoxan tests. The epinephrine level in the blood was reported to be high. Excretory urograms were negative. Operation was performed. The right adrenal gland and an attached tumor were removed. The tumor was reported to be a benign pheochromocytoma. Phentolamine was used to control the blood pressure both preoperatively and during the operation. The patient was relieved of the symptoms after the operation.

CASE 17 (Litman and State,[42] 1949).—A girl, aged 11 years, was admitted to the hospital in a convulsive state following an acute febrile episode. Her urine contained abnormal amounts of albumin, casts, and red blood cells. The blood pressure on admission was 174/100. The diagnosis at that time was acute glomerulonephritis. The clinical picture during the hospitalization was characterized by perspiration, polydipsia, polyuria, lethargy, and amnesia. On further questioning it was found that she had had frequency of urination and nocturia following an attack of scarlet fever two years previously. The patient also had had attacks of headache, nausea, and vomiting once or twice a year since the age of 2. Both N,N-dibenzyl-β-chloroethylamine (Dibenamine) and piperoxan tests were positive. Excretory urogram was reported negative. Exploration was carried out through a

right rectus incision. A tumor was found involving the right adrenal gland. Blood pressure dropped precipitously, and the patient died after the enucleation of the tumor. The pathological diagnosis was pheochromocytoma.

CASE 18 (Seelmann,[64] 1950).—A white girl, aged 13 years, complained of headache, nausea, pallor, and weight loss for six years. These symptoms, associated with weakness, sweating, and pain in the chest and abdomen, became worse three months prior to admission. Disturbances of vision were noticed for two weeks. Papilledema, exudates, and petechiae were present in the eyegrounds. The blood pressure was elevated to 230/140. ECG showed evidence of myocardial damage. Perirenal air insufflation and retrograde and intravenous pyelograms did not reveal any abnormality. An abnormally high adrenalin level was found in the blood. A tumor of the right adernal medulla was found and removed at operation. The patient died 30 hours after the operation. A second tumor was discovered in the left adrenal gland at necropsy. Pathological diagnosis of both tumors was pheochromocytoma.

CASE 19 (Koffler, [37] 1950).—A Negro boy, aged 12 years, was admitted to the hospital three times, between November, 1946, and August, 1947, with the chief complaints of headache, vomiting, disorientation, and convulsions. Blood pressure was elevated, ranging between 150/100 and 208/158. Physical examination revealed cardiomegaly, weak left extremities, and eyeground changes. Spinal fluid pressure was elevated. Urine specific gravity was consistently low, and albumin was present in the urine. A diagnosis of chronic glomerulonephritis with hypertensive cardiovascular disease was made. The patient was next seen two years later (April, 1949), when he was admitted in a stuporous state with a spastic left hemiplegia. Blood pressure was 240/180 on admission. Piperoxan and Dibenamine tests were performed and were found positive. A right adrenal tumor, identified as a pheochromocytoma, was removed at operation. The patient was checked six months after operation and was found to have a blood pressure of 120/80. He was doing very well but was walking with a slight limp.

CASE 20 (McCoy and Bridgeman,[44] 1950).—A white girl, aged 13 years, was referred for studies because of hypertensive changes in the eyegrounds discovered by an ophthalmologist during the fitting of glasses. The patient complained of failing vision for about a year. She also had episodes of headache, sweating, and pain in the lumbar region starting a year and a half previously. Hypertension around 210/160 was present in all four extremities, accompanied by hypertensive retinopathy. The blood pressure tended to vary with posture but never came down to the normal range spontaneously. However, both piperoxan and Dibenamine caused marked drop in the blood pressure. Intravenous pyelogram revealed a moderate indenture of the pelvis of the left kidney. Operation was done through a left paravertebral incision, and a tumor of the left adrenal gland was removed. Moderately high blood pressure, around the level of 150/110, was present for several weeks following the operation. Repeated tests with piperoxan, Dibenamine, and histamine were all negative. When she was seen eight months later the patient's blood pressure was normal.

CASE 21 (Brachetto-Brian and Brewer,[9] 1950).—This is the case report of a 13-year-old boy with pheochromocytoma. The original article could not be obtained.

CASE 22 (Hubble,[31] 1951).—A boy, aged 11½ years, began having attacks of abdominal pain, vomiting, sweating, and palpitation about five years before admission. These symptoms were soon followed by intermittent nocturnal enuresis, pain in the eyes, and photophobia. His vision was greatly impaired. He appeared restless, active, and pale, with attacks of sweating and tachycardia. His heart was enlarged, with presence of prominent murmurs and a thrill. ECG showed left ventricular strain pattern. The blood pressure varied between 150 and 240 systolic and 100 and 150 diastolic. A positive response was obtained with piperoxan test. Since other studies were unrevealing, an exploratory laparotomy was performed. A tumor in the right adrenal gland and possibly another one near the tail of the pancreas were palpated. The tumors were not removed. The patient died suddenly seven hours after the operation. At necropsy a pheochromocytoma was found associated with each adrenal gland. Two smaller accessory tumors of a similar nature were also found in front of the aorta.

CASE 23 (Berkheiser and Rappoport,[6] 1951).—A white girl, aged 11 years, was one of the five cases of unsuspected pheochromocytoma reported by these authors. She was admitted to the hospital because of facial edema, excessive sweating, and high blood pressure. Her mother had died of malignant hypertension (?). The essential positive findings were a high blood pressure, of 180/135; large heart with thrill and murmur, and 3+ albumin in the urine. She was discharged with the diagnosis of chronic glomerulonephritis and secondary hypertension. During the six months of bed rest at home her blood pressure was between 140/100 and 180/150. She was readmitted five years later in a semistuporous and irrational state, with spastic paralysis of the left half of the body. Blood pressure on admission was 220/130. Patient died three hours after admission. Necropsy revealed

atherosclerosis of the aorta, coronary, and cerebral arteries and sclerosis of the renal arteries; fresh hemorrhage in the ventricles of the brain, and a small pheochromocytoma in the medulla of the left adrenal gland.

CASE 24 (Bastrup-Madsen,[2] 1951).—A girl, aged 9 years, died of acute poliomyelitis. At necropsy a left suprarenal pheochromocytoma and hypertrophy of the left ventricle was found.

Two years before her death she had been hospitalized with attacks characterized by vertigo, drowsiness, spasms in the upper limbs, and sometimes a feeling of oppression in the chest. Blood pressure was not taken during an attack; however, it was normal between the attacks. She stopped having these attacks while in the hospital and was dismissed as a case of neurosis.

CASE 25 (Faber,[21] 1951).—A girl, aged 13 years, gave a history of paroxysmal headaches of four to five months' duration. Two weeks prior to admission she developed visual disturbances and was found to have albuminuria and hypertension. Positive response was obtained with piperoxan test. An orange-sized pheochromocytoma was removed at operation.

CASE 26 (Iseri,[32] 1951).—A Negro boy, aged 8 years, had had episodes of sweating and precordial pulsation for about one year. Weight loss was also noticed, despite a ravenous appetite. One month prior to admission he developed headache, frequency of urination, abdominal pain, vomiting, and poor vision. Blood pressure on admission was 210/170 in the arm and 260/200 in the leg. Marked hypertensive retinopathy was observed in both fundi. On deep palpation a mass was felt in the left upper quadrant of the abdomen. BMR was +31%. Urine showed trace of albumin. ECG showed left ventricular ischemia. Intravenous and retrograde pyelograms revealed evidence of a mass displacing the left kidney laterally. Massage of the left lumbar region caused a rise in blood pressure. Therapeutic tests with piperoxan and phentolamine given intramuscularly, intravenously, and orally all resulted in definite drop of the blood pressure. The patient was kept on oral phentolamine for three weeks before operation, with marked improvement in the symptoms. Laparotomy revealed a tumor medial to the lower pole of the left kidney. Both adrenal glands appeared normal. The tumor was removed and was diagnosed as malignant pheochromocytoma. Chemical analysis of its extract showed a higher content of arterenol than of epinephrine.

CASE 27 (Apter,[1] 1951).—A white girl, aged 14 years, for one year had had episodes of dyspnea, headache, and palpitation. She also complained of weakness, loss of weight, and failing vision during that period. Her mother died of high blood pressure and diabetes, one month prior to her admission. Eyeground examination disclosed papilledema, vascular changes, and hemorrhages. Her heart was enlarged to the left, and blood pressure was 250/160. BMR was +20% to +41%. Urea clearance was 50% of normal. Glucose tolerance test showed a diabetic curve. Positive response was observed with piperoxan test. A pheochromocytoma was removed at operation from the region of right adrenal gland. All abnormal symptoms had disappeared when she was checked seven months after the operation.

CASE 28 (Soffer,[60] 1951).—A boy, aged 7 years, who had extra-adrenal paraganglioma was mentioned by Soffer in his book, but with no detailed description.

CASE 29 (Neill and Smith,[54] 1952).—A boy, aged 6 years, had been ill for six weeks with lethargy and attacks of night sweats which were usually preceded by pallor and headache. The blood pressure on admission was 190/133. He appeared thin and anxious. His hands were cold and sweating and showed desquamation, closely simulating acrodynia. Albumin was present in the urine. BMR was +145%. A piperoxan test was done but showed no satisfactory response. X-ray studies revealed suspicious shadows above each kidney. The patient was discharged without a definitive diagnosis and was readmitted 10 months after the onset of the illness. He died suddenly during the passage of an urethral dilator, while he was anesthetized. At necropsy a tumor was found in each of the adrenal glands, both arising from the medulla, showing the characteristic of pheochromocytoma.

CASE 30 (Talbot,[72] 1952).—A white boy, aged 6 years, had bilateral pheochromocytoma, was operated upon, but died later.

CASE 31 (Klein,[35] 1953).—A boy, aged 11 years, ill for three and one-half years, presented a picture of posterior fossa tumor accompanied by retardation of growth and loss of weight. His blood pressure was constantly high (200/170 mm. Hg). A benign pheochromocytoma of the left adrenal gland was found on necropsy, which also revealed generalized atherosclerosis, thrombosis and encephalomalacia of the brain, and hypertrophy of the left heart chamber.

CASE 32 (Goldfarb,[25] 1953).—A Negro boy, aged 9 years, was brought to the hospital because of severe cough of three to four weeks' duration. Along with the cough, he also developed frequency of urination, constipation, and bouts of weakness and sweating. On examination the heart was found to be enlarged, especially the left ventricle, and the liver was palpated 2 fingerbreadths below the costal margin. ECG showed evidences of left axis deviation and myocardial disease. During hos-

pitalization, he had moderate elevation of temperature and tachycardia; his blood pressure varied between 110/90 and 170/140. The constipation became progressively worse and finally led to signs of intestinal obstruction. The patient went into congestive heart failure and died after an enema given under pressure. X-ray studies to search for pheochromocytoma were not carried out before death because of the severe constipation and congestive heart failure. Malignant pheochromocytomas were found in both adrenal glands on necropsy.

Case 33 (Berg,[5] 1953).—A boy, aged 15 years, was admitted to the hospital with the complaint of severe headaches in the frontal and occipital regions of two to three months' duration. He was found to have a blood pressure of 220/160 on admission. Papilledema and hemorrhages were observed in the eyegrounds. Urinalysis showed presence of albumin. Blood urea was elevated, and BMR was +11.8%. While in the hospital he had attacks of severe headache associated with abdominal pain, pallor, and cold skin, terminating with profuse sweating. Abdominal exploration of both adrenal regions and aorta did not yield any findings. Operation was terminated because the patient's condition deteriorated. He died after the operation. At necropsy a pheochromocytoma was found in the right adrenal gland, and a small tumor was found near the left adrenal gland.

Case 34 (Wen and Fu,[76] 1953).—A Chinese boy, aged 14 years, was admitted to the hospital with the symptoms of headaches, dizziness, sweating, fever, and convulsions of three days' duration. His blood pressure on admission was 116/80; it rose to 170/130 on the third day after the admission. Funduscopic examination revealed the presence of exudates and hemorrhages in both eyes. A vague mass was palpated in the right renal region, which was confirmed by perirenal air insufflation to be just above the right kidney. A clinical diagnosis of pheochromocytoma was made, but operation was refused and the patient was discharged against advice.

Case 35 (Schafer,[61] 1954).—A white boy, aged 10 years, had been suffering from headache and vomiting for six weeks and from moderate dyspnea on exertion for four weeks. The headache was intermittent at first but later became constant. The patient was of asthenic build. Examination of the fundi revealed bilateral papilledema, hemorrhages, and arteriospasm. Blood pressure ranged between 240 and 300 systolic and 150 and 170 diastolic. Trace of albumin was present in the urine. The patient died suddenly one week after admission. Necropsy revealed three tumor masses in the right adrenal gland, all composed of large polygonal cells with granular acidophilic cytoplasm and small hyperchromatic nuclei.

Case 36 (Israelski,[32] 1954).—A boy, aged 10 years, was admitted to the hospital with a nine months' history of loss of weight; listlessness; excessive sweating, particularly at night; thirst, and polyuria. For one month he had complained of frontal headaches, occasionally associated with vomiting.

The patient's father had died at the age of 23 years with a history of excessive sweating since the age of 16 years, and for 6 months before death he had also complained of impaired vision. On examination, he was found to have slight papilledema, blood pressure of 210/170, and albumin, red blood cells, and casts in the urine. He apparently died of a cerebral accident.

Physical examination of the patient revealed him to be thin, pale, and anxious in expression. He had moist skin and dull red discoloration of both hands. His blood pressure had wide spontaneous fluctuations, with the highest reading being 250/180. A drop of over 60 mm. Hg in the blood pressure was obtained with the piperoxan test. Arterenol was excreted in the urine at the rate of 2000γ in 24 hours. Extraperitoneal pneumography demonstrated clearly a tumor at the upper pole of the right kidney. The tumor was removed through a right lumbar incision. During the operation, piperoxan was given before and arterenol, after the removal of the tumor to control the blood pressure. The tumor was identified histologically as typical pheochromocytoma. All symptoms subsided after the operation.

Case 37 (Negri and Vanoni,[68] 1954).—A white boy, aged 12 years, had headaches, vomiting, sweating, and abdominal pains for about one year. Funduscopic examination revealed papilledema, hemorrhages, and exudates. A sustained but slightly fluctuating hypertension was present. BMR was +38%. Both piperoxan and phentolamine tests gave a positive response. The urinary content of arterenol was abnormally high. Retroperitoneal pneumography outlined a large mass just above the right kidney. Pheochromocytoma was suspected and was later confirmed by surgery. Blood pressure was controlled by piperoxan and arterenol during the operation. The postoperative course was uneventful. When last seen, six months after the operation, he was symptom-free, except for some exudates in the eyegrounds.

Case 38 (Popper and Theron,[59] 1954). This is the case report of a 13-year-old Bantu boy, with a successful surgical removal of a right adrenal tumor. The original article could not be obtained.

Case 39 (Weiman,[78] 1954).—A white girl, aged 14 years, complained of headache for four months. Her illness started about nine months before admission to the hospital with episodes of gingival

bleeding. The blood pressure was reported to have been normal at that time. Headache was constant in the occipital region. She developed nausea and vomiting, and weight loss of almost 20 lb. occurred within a period of three months. She appeared tense and had periods of diaphoresis. Papilledema and vascular changes were present in the eyegrounds. Blood pressure on admission was 190/155 in the arms and 220/190 in the legs but fluctuated widely during hospitalization. BMR was +83%. ECG showed evidences of left ventricular hypertrophy. Positive response was obtained with both piperoxan and tolazoline (Priscoline) tests. Urine of the patient when injected into the vessels of a dog consistently caused a rise in the blood pressure. A mass medial to the right kidney was demonstrated by retroperitoneal pneumography. The tumor was removed through a transverse abdominal incision. The immediate drop in the blood pressure was controlled by epinephrine, while arterenol and phenylephrine (Neo-Synephrine) had little effect. Extract of the tumor caused a rise of blood pressure when injected into a dog. The patient died of Staphylococcus albus septicemia and peritonitis 11 days after operation.

CASE 40 (Daeschner,[15] 1954).—A white boy, aged 4 years, became ill two and one-half years prior to hospitalization with thirst, enuresis, constipation, and failure to gain weight in spite of good appetite. One year later excessive sweating and polydipsia occurred. His personality was characterized by extreme emotional lability. For six months before admission he suffered from severe paroxysmal headaches in addition to the above symptoms, which became more pronounced. At the time of admission the patient was small for his age and appeared anxious. His blood pressure was 180/115. His hands were puffy and plethoric. Funduscopic examination was negative, except for vascular spasm. ECG suggested left and right ventricular hypertrophy. Intravenous pyelogram showed downward displacement of the right kidney and indentation of its superior pole. Presacral air injection clearly outlined a mass at the right adrenal gland region. Both piperoxan and phentolamine tests before the operation yielded positive response. The patient was put on a regimen of oral phentolamine, which greatly ameliorated all abnormal symptoms and signs. An operation was performed 10 days later, and a right adrenal tumor was removed without difficulty. Renal hemodynamic studies demonstrated a decrease in the renal vascular resistance after the operation. The pathological diagnosis was ganglioneuropheochromocytoma. The patient remained asymptomatic to the time of the report, 15 months later.

CASE 41 (Schleisner,[62] 1954).—This is the report of a child with bilateral pheochromocytoma. The original article could not be obtained.

CASE 42 (Manger,[40] 1954).—A boy, aged 12 years, was cited as 1 of 13 cases of pheochromocytoma in which chemical quantitation of the pressor amines in the plasma was carried out. There was a history of headaches and known hypertension for five months and nosebleeds, easy sweating, and weight loss for three months. Two months before hospitalization he had a left-sided convulsion. Examination of the eyegrounds showed advanced hypertensive retinopathy. Determination of the pressor amines in the plasma before the operation was as follows: epinephrine-like substance, 6.1γ/liter; epinephrine, 1.6γ/liter; arterenol, 14.1γ/liter. After removal of the tumor, the values were 1.6, 0.1, and 4.6, respectively. Preoperative blood pressure was 195/145, and postoperative blood pressure was 130/85.

CASE 43 (Lukemeyer,[43] 1954).—A white boy, aged 7 years, had attacks of headaches, sweating, dyspnea, cyanosis, and vomiting for five to six months. He lost about 20 lb. during that period, and bed-wetting also developed. He was admitted to the hospital in cardiac failure. Blood pressure was 200/120. Examination also revealed papilledema, exudates, and hemorrhages in the eyegrounds. A positive response was obtained with a piperoxan (Benodaine) test. A pheochromocytoma of the right adrenal gland was removed surgically. During the operation cardiac arrest occurred, and the patient was revived by cardiac massage. He remained unconscious for six days following the operation. At the time of discharge he had left hemiparesis and aphasia, but the blood pressure was normal.

CASE 44 (Snyder and Rutledge,[67] 1955).—A white boy, aged 13 years, gave a history of headaches, loss of weight, nervousness, easy fatigability, and excessive perspiration for eight months. On admission, he appeared pale, anxious, and emaciated. Blood pressure was 208/160 in the arm and 180/134 in the leg. Papilledema and hemorrhages were observed in the eyegrounds. BMR was +54%. A transient hypercalcemia was observed, without explanation. A number of subcutaneous masses which had been present for three to four years were subsequently proved to be neurofibromas by biopsy. Tests with phentolamine and piperoxan caused marked drop in the blood pressure. He was maintained on a course of phentolamine orally before surgery. Excretory urogram and presacral pneumogram failed to help the diagnosis. A mass above the right kidney was finally localized by translumbar aortography. The tumor was removed through a right flank incision and was identified as a benign pheochromocytoma. The patient revealed no abnormal symptoms when examined two months after surgery.

CASE 45 (Smid and DuShane,[65] 1955).—A white boy, aged 12 years, presented a history of headaches for five months, epistaxis for six weeks, and vomiting for four weeks, associated with loss of appetite and loss of weight. There was one episode of convulsion followed by semistupor for two days. Bilateral papilledema and vascular changes were observed in the eyegrounds. Grade 1 to 3 albumin was present in the urine. BMR was +9%. Two phentolamine tests done on consecutive days showed positive response. A pheochromocytoma was removed from the left adrenal gland at operation. It yielded epinephrine and arterenol on chemical analysis. Blood pressure returned to normal after the operation, and other symptoms were regressing at the time of dismissal.

CASE 46 (Young and Murray,[78] 1955).—A boy, aged 15 years, was investigated for headache, glycosuria, and hypertension. Both piperoxan and Dibenamine tests gave positive responses. A pheochromocytoma was removed surgically. However, the blood pressure rose again and then gradually fell off for several weeks following the operation. The patient was found to be symptom-free two and a half years later.

CASE 47 (Young and Murray,[78] 1955).—A girl, aged 12 years, the sister of the boy in Case 46, was admitted to the hospital because of severe headache, restlessness, weakness, and vomiting of two weeks' duration. She had a convulsion followed by left hemiparesis and coma on the third day after admission to the hospital. She died the same day. Necropsy revealed a pheochromocytoma.

SUMMARY

A case of pheochomocytoma in an 8-year-old boy is reported. Polydipsia and polyuria were the presenting symptoms for 18 months, during which time he was treated as a case of diabetes inspididus. After admission he was observed to have sustained hypertension. Piperoxan and phentolamine (Regitine) tests were positive. The tumor was localized in the right adrenal region by retroperitoneal pneumograms made with presacral injection of air. Phentolamine was given orally for 48 days preoperatively, with improvement in the symptoms. The tumor was removed, and the postoperative course was uneventful. At the time of this writing, six months after the operation, patient is symptom-free and doing well.

A brief review of the literature is presented. A total of 47 other cases of pheochromocytoma occurring in patients under 16 years of age are collected and summarized from the world literature.

Dr. Thomas F. FitzGerald and Dr. George Schuster III performed the operation. Dr. John K. Kohlhaas was the anesthetist. Dr. C. B. Slabaugh and Dr. C. R. Little did the ophthalmologic examinations.

REFERENCES

1. Apter, N. S.; Halstead, W. C.; Alving, A. S.; Talso, P. T., and Case, T. J.: Alterations of Cerebral Functions in Pheochromocytoma, Neurology **1**: 283, 1951.

2. Bastrup-Madsen, P.: A Case of Phaeochromocytoma in a Child, Ugesk. læger **113**:420, 1951.

3. Belt, A. E., and Powell, T. O.: Clinical Manifestations of the Chromaffin Cell Tumors Arising from the Suprarenal Medulla, Surg. Gynec. & Obst. **59**:9, 1934.

4. Berdez: Contribution a l'étude des tumeurs des capsules surrenales, Arch. méd. exper. et anat. path. **4**:414, 1892.

5. ten Berg, J. A. G.: Case of Pheochromocytoma, Nederl. tijdschr. geneesk. **97**:2967, 1953.

6. Berkheiser, S. W., and Rappoport, A. E.: Unsuspected Pheochromocytoma of the Adrenal: Report of 5 Cases, Am. J. Clin. Path. **21**:657, 1951.

7. Biebl, M., and Wichels, P.: Physiologische und pathologisch-anatomische Betrachtungen in Anschluss an einen Fall von Paragangliom beider Nebennieren, Arch. path. Anat. **257**:182, 1925.

8. Blackwood, J.: Presacral Perirenal Pneumography, Brit. J. Surg. **39**:111, 1951.

9. Brachetto-Brian, D., and Brewer, E.: Paraganglioma adrenal con hipertensión y nefrosclerosis consecutiva en un niño de 13 años, An. Inst. med. exper. **2**:201, 1950.

10. Brewer, E. C. B.: Cromafinomas en niños, Arch. argent. pediat. **31**:138, 1949.

11. Bruce, G. M.: Changes in the Ocular Fundus Associated with Pheochromocytoma of Adrenal Gland: Report of 3 Cases, Arch. Ophth. **39**:707, 1948.

12. Brunschwig, A., and Humphreys, E.: Excision of Pheochromocytoma, J. A. M. A. **115**:355, 1940.

13. Cahill, G. F.: Pheochromocytomas, J. A. M. A. **138**:180, 1948.

14. Calkins, E., and Howard, J. E.: Bilateral Familial Pheochromocytoma with Paroxysmal Hypertension, J. Clin. Endocrinol. **7**:475, 1947.

15. Daeschner, C. W.; Moyer, J. H., and Able, L. W.: Pheochromocytoma in a 4-Year-Old Child: Renal Hemodynamic, Pharmacologic, and Radiographic Studies, J. Pediat. **45**:141, 1954.

16. Davis, F. W., Jr.; Hull, J. G., and Vardell, J. C., Jr.: Pheochromocytoma with Neurofibromatosis, Am. J. Med. **8**:131, 1950.

17. Eisenberg, A. A., and Wallerstein, H.: Pheochromocytoma of Suprarenal Medulla, Arch. Path. **14**:6, 1932.

18. Espersen, T., and Dahl-Iversen, E.: The Clinical Picture and Treatment of Pheochromocytomas of the Suprarenal, Acta chir. scandinav. **94**: 271, 1946.

19. Evans, V. L.: Suprarenal Tumor with Paroxysmal Hypertension, J. Lab. & Clin. Med. **22**: 1117, 1937.

20. Evans, W. F., and Stewart, H. J.: Peripheral Blood Flow in Case of Pheochromocytoma Before and After Surgery, Am. Heart J. **24**:835, 1942.

21. Faber, M.: Benzodioxan-Test for Phaeochromocytoma, Ugesk. læger **113**:413, 1951.

22. Fränkel, F.: Ein Fall von doppelseitigem völlig latent verlaufenen Nebennierentumor und gleichzeitiger Nephritis mit Veränderungen am Circulationsapparat und Retinitis, Arch. path. Anat. **103**:244, 1886.

23. Ganem, E. J., and Cahill, G. F.: Pheochromocytomas Co-Existing in Adrenal Gland and Retroperitoneal Space with Sustained Hypertension, New England J. Med. **238**:692, 1948.

24. Goldenberg, M.; Snyder, C. H., and Aranow, H., Jr.: New Test for Hypertension Due to Circulating Epinephrine, J. A. M. A. **135**:971, 1947.

25. Goldfarb, P. M.: Pheochromocytoma: Report of Case in 9 Year Old Negro Male, J. M. A. Alabama **23**:70, 1953.

26. Gørtz, G.: Pheochromocytoma, Nord. med. **26**:1277, 1945.

27. Graham, J. B.: Pheochromocytoma and Hypertension: An Analysis of 207 Cases, Surg. Gynec. & Obst. **92**:105, 1951.

28. Grimson, K. S.; Longino, F. H.; Kernodle, C. E., and O'Rear, H. B.: Treatment of a Patient with a Pheochromocytoma: Use of an Adrenolytic Drug Before and During Operation, J. A. M. A. **140**:1273, 1949.

29. Harbitz, F.: Tumors of the Sympathetic Nervous System and the Medulla of the Suprarenal Glands, Especially Malignant Neuroblastomas, Arch. Int. Med. **16**:324, 1915.

30. Helly, K.: Zur Pathologie der Nebenniere, Munchen. med. Wchnschr. **60**:1811, 1913.

31. Hubble, D.: Pheochromocytoma in Children, Arch. Dis. Childhood **26**:340, 1951.

32. Iseri, L. T.; Henderson, H. W., and Derr, J. W.: Use of Adrenolytic Drug, Regitine, in Pheochromocytoma, Am. Heart J. **42**:129, 1951.

33. Israelski, M.; Kendall, A. C., and Shaw, R. E.: A Case of Pheochromocytoma in Childhood, Arch. Dis. Childhood **29**:18, 1954.

34. Kirshbaum, J. D., and Balkin, R. B.: Adrenalin-Producing Pheochromocytoma of Adrenal Associated with Hypertension: Report of 3 Cases, Ann. Surg. **116**:54, 1942.

35. Klein, F.; Albrecht, P., and Žucha, J.: Pheochromocytoma as a Cause of Chronic Hypertension in an 11-Year-Old Boy, Časop. lék. česk. **92**:571, 1953.

36. Knake, E.: Über einen Fall von doppelseitigem Pheochromocytom der Nebenniere und die Bedeutung des Adrenalins in klinischen Bilde dieser Geschwülste, Arch. path. Anat. **308**:615, 1942.

37. Koffler, I.; Buck, G.; Wingard, C.; Hitchcock, P.; Guthrie, R., and Teague, R. S.: Diagnosis by the Benzodioxane Test, Urinary Hormone Studies, and Nor-Epinephrine Assay of the Tumor, J. Clin. Endocrinol. **10**:897, 1950.

38. Kremer, D. N.: Medullary Tumor of the Adrenal Glands with Hypertension and Juvenile Arteriosclerosis, Arch. Int. Med. **57**:999, 1936.

39. L'Abbé, M.; Tinel, J., and Doumer: Crises solaires et hypertension paroxystique en rapport avec une tumeur surrénale, Bull. et. mém. Soc. méd. hôp. Paris **46**:982, 1922.

40. Linde, P.: Unusual Tumor (Pheochromocytoma) in Infant 5 Months Old, Nord. med. **13**: 897, 1942.

41. Linneweh, F.: Über eine seltene Form des blassen Hochdrucks, Monatsschr. kinderh. **90**:179, 1942.

42. Litman, N. N., and State, D.: Pheochromocytoma: Use of N,N-Dibenzyl-Betachloroethylamine and Piperidino-Methylbenzodioxane (Benzodioxane) in Surgical Therapy, Pediatrics **4**:735, 1949.

43. Lukemeyer, G. T.: Pheochromocytoma: Case Report of Diagnosis and Surgical Cure, J. Indiana M. A. **47**:1377, 1954.

44. McCoy, G. E., and Bridgeman, M. L.: Use of Drugs in Diagnosis and Treatment of Pheochromocytoma, Pediatrics **6**:286, 1950.

45. MacKeith, R.: Adrenal-Sympathetic Syndrome: Chromaffin Tissue Tumor with Paroxysmal Hypertension, Brit. Heart J. **6**:1, 1944.

46. MacKenzie, D. W., and McEachern, D.: Tumor of Medulla of Adrenal (Adrenal Pheochromocytoma) with Removal and Relief of Paroxysmal Hypertension, J. Urol. **40**:467, 1938.

47. Manasse, P.: Über die hyperplastischen Tumoren der Nebennieren, Arch. path. Anat. **133**: 391, 1893.

48. Manasse, P.: Zur Histologie und Histogenese der primaren Nierengeschwulste, Arch. path. Anat. **145**:127, 1896.

49. Manger, W. M.; Flock, E. V.; Berkson, J.; Bollman, J. L.; Roth, G. M.; Baldes, E. J., and Jacobs, M.: Chemical Quantitation of Epinephrine and Norepinephrine in 13 Patients with Pheochromocytoma, Circulation **10**:641, 1954.

50. Marchetti, G.: Beitrag zur Kenntniss der pathologischen Anatomie der Nebennieren, Arch. path. Anat. **177**:227, 1904.

51. Masson, P., and Martin, J. F.: Paragangliome surrénal: Étude d'un cas humain de tumeurs malignes de la médullo-surrénal, Bull. Assoc. franç. étude cancer **12**:135, 1923.

52. Neff, F. C.; Tice, G.; Walker, G. A., and Ockerblad, N.: Adrenal Tumor in Female Infant with Hypertrichosis, Hypertension, Overdevelopment of External Genitalia, Obesity, but Absence of Breast Enlargement, J. Clin. Endocrinol. **2**:125, 1942.

53. Negri, M., and Vanoni, R. P.: A propos d'un cas de pheochromocytome chez un enfant de 12 ans, Helvet. pædiat. acta **9**:1, 1954.

54. Neill, C. A., and Smith, G.: Bilateral Phaeochromocytoma in a 6-Year-Old Boy, Arch. Dis. Childhood **27**:286, 1952.

55. Neusser, E., and Wiesel, J.: Die Erkrankungen der Nebennieren, Ed. 2, Vienna, Alfred Holder, 1910, p. 97.

56. Pick, L.: Das Ganglioma embryonale sympathicum, Berl. klin. Wchnschr. **49**:16, 1912.

57. Pincoffs, M. C.:, A Case of Paroxysmal Hypertension Associated with Suprarenal Tumor, Tr. A. Am. Physicians **44**:295, 1929.

58. Poll, H.: Die vergleichende Entwicklung der Nebennierensysteme, in Hertwig, W. A. O.: Lehrbuch der Entwicklungsgeschichte des Menschen und der Wirbelthiere, Jena, Gustav Fischer, 1906, Vol. 3, p. 442.

59. Popper, E. N., and Theron, P.: Phaeochromocytoma in a Bantu Child, South African M. J. **28**: 286, 1954.

60. Rabin, C. B.: Chromaffin Cell Tumor of Suprarenal Medulla (Pheochromocytoma), Arch. Path. Chicago **7**:228, 1929.

61. Schaefer, R. L.; Schaefer, R. L., Jr., and Christopher, J.: Pheochromocytoma with Hypertension in Childhood, J. Michigan M. Soc. **53**:75, 1954.

62. Schleisner, P.: Bilateral Pheochromocytoma in Child: The Differential Diagnosis from Nephritis, Danish M. Bull. **1**:142, 1954.

63. Shipley, A. M.: Paroxysmal Hypertension Associated with a Tumor of the Adrenal, Ann. Surgery **90**:742, 1929.

64. Seelemann, K.: Das Phaeochromocytom im Kindesalter und seine Beziehungen zum Hochdruck, Ztschr. Kinderh. **68**:191, 1950.

65. Smid, A. C., and DuShane, J. W.: Pheochromocytoma in Children: Report of Case, Am. J. Dis. Child. **90**:81, 1955.

66. Smithwick, R. H.; Greer, W. E. R.; Robertson, C. W., and Wilkins, R. W.: Pheochromocytoma: A Discussion of Symptoms, Signs, and Procedures of Diagnostic Value, New England J. Med. **242**:252, 1950.

67. Snyder, C. H., and Rutledge, L. J.: Pheochromocytoma: Localization by Aortography, Pediatrics **15**:312, 1955.

68. Snyder, C. H., and Vick, E. H.: Hypertension in Children Caused by Pheochromocytoma: Report of 3 Cases and Review of the Literature, Am. J. Dis. Child. **73**:581, 1947.

69. Soffer, L. J., and Gabrilove, J. L.: Pheochromocytoma and Paraganglioma of the Adrenal, in Diseases of the Endocrine Glands, Philadelphia, Lea & Febiger, 1951, pp. 387-403.

70. Suzucki, S.: Über einen chromaffinen Tumor des Nebennierenmarks, Berl. klin. Wchnschr. **46**: 1644, 1909.

71. Suzucki, S.: Über 2 Tumoren aus Nebennierenmarkgewebe, Berl. klin. Wchnschr. **47**:1623, 1910.

72. Talbot, N. B.; Sobel, E. H.; McArthur, J. W., and Crawford, J. D.: Functional Endocrinology from Birth Through Adolescence, Cambridge, Mass., Harvard University Press, 1952, pp. 271-289.

73. Vaquez, H., and Donzelot, E.: Les crises d'hypertension arterielle paroxystique, Presse méd. **34**:1329, 1926.

74. Wahl, H. R.: Neuroblastoma: With a Study of a Case Illustrating the 3 Types That Arise from the Sympathetic System, J. M. Res. **25**:205, 1914.

75. Weiman, C.; Back, K.; Russo, P. E.; Shoemaker, H. A., and Wolf, S.: The Diagnosis of Pheochromocytoma by Demonstration of Pressor Substances in the Urine and by Retroperitoneal Pneumography, Ann. Int. Med. **41**:131, 1954.

76. Wen, S. Y., and Fu, S. S.: Pheochromocytoma: A Brief Review and Report of 2 Cases, Chinese M. J. **71**:399, 1953.

77. Wiesel, J.: Der heutige Stand der Lehre von der Arteriosklerose, Wien. klin. Wchnschr. **22**:401, 1909.

78. Young, W. S., and Murray, W. A.: Familial Adrenal Pheochromocytoma with Sustained Hypertension, Canad. M. A. J. **72**:503, 1955.

Case Reports

TYPHOID WITH MENINGITIS (SALMONELLA TYPHOSA)

Report of Case in Infant with Recovery

SAM M. POWELL, M.D., Corpus Christi, Texas

TYPHOID with typhoid (Salmonella typhosa) meningitis is rare and an extremely grave disease, considered fatal in newborn infants.* Kantor [5] states that he knows of only two cases of Salmonella meningitis in babies under one month of age who recovered; neither, however, was caused by S. typhosa. Ripy's patient was over a year old. Henderson [6] has an excellent and comprehensive collection of 144 Salmonella meningitis cases; he added 3 of his own, making a total of 147 of all types, but omitted a case of S. typhosa, which Beene and coworkers [7] include. He mentions the frequency of pneumonitis or bronchitis, the presence or absence of gastrointestinal symptoms, and the frequency of meningococcic meningitis preceding the Salmonella infections. Beene, Hansen, and Fulton [7] have references to 87 additional cases of Salmonella meningitis of various types reported since Henderson [6] in describing their first known case of Salmonella sp. (Type Montevideo) meningitis. The mortality in these 87 cases was 72, or 80%. Some of these reports described cases of typhoid in which the onset was characterized by symptoms of acute meningitis, and it was not until adequate bacteriological study that they were revealed to be cases of typhoid, without the usual enteric manifestations.

It is believed that this is the youngest patient with S. typhosa meningitis to survive and the one case of the few cases of survival reported in the literature.

Submitted for publication Feb. 21, 1953.

From the Pediatric Service of the Memorial Hospital.

* References 1, 2, 3, 4, and 6.

REPORT OF CASE

A white girl aged 26 days was admitted to Memorial Hospital on Aug. 19, 1952, with the chief complaint of convulsions for 24 hours, intermittent fever with cough since the age of 19 days, and collapse.

Family History.—Both parents and a 3-year-old sibling were living and well. None had had any diseases suggestive of typhoid fever.

Social History.—Several cases of typhoid had been reported in the patient's home town, one of which occurred in a trailer camp two blocks from her home after the patient's admission. The parents were above average intellectually and economically.

Present Illness.—The patient was born at term in Kingsville, Texas, in the Kingsville Hospital, on July 24, 1952, of an unipara and secundagravida Rh-positive mother. The birth weight was 2892 gm. There were no neonatal complications, and she went home on July 27 and was given a 1:2 evaporated-milk-water formula prepared by accepted sterilization technique. She was seen at weekly intervals by her family physician in his office for newborn examinations. On Aug. 13, when she was aged 19 days, a cough and fever developed. The following morning her temperature was 102 F. rectally after administration of 60 mg. of acetylsalicylic acid. Her physician told the parents she had a possible pneumonia, and she was admitted to the Kingsville Hospital and given injections of penicillin and dihydrostreptomycin intramuscularly for two days. She was discharged on Aug. 16, 1952, improved, and taking chlortetracycline (Aureomycin) spersoids, 50 mg. every six hours for six doses. There was no history of diarrhea, vomiting, distention, skin rash, rose spots, or convulsions. Two days later, Aug. 18, she refused to nurse and had profuse perspiration. Later in the day she began to have convulsive movements, first of her hands and arms, becoming generalized about 7 p. m. Her physician hospitalized her again and partially controlled the convulsions during the night with secobarbital (Seconal) suppositories. Her temperature rose during the night, and she was sent to my office the following morning, at which time her temperature was 102 F., and she was comatose and having a generalized convulsion. She was given 30 mg.

of phenobarbital sodium intramuscularly and transported to Memorial Hospital, with oxygen being given by a nasal catheter.

Physical Examination.—This was an acutely ill moribund baby girl with ashen color, feeble pulse, and generalized clonic convulsions of the face, eyelids, and extremities. The temperature was 102 F, the pulse rate, 210, and the respirations, 50, rapid, and shallow. Her weight was 3000 gm. The anterior fontanelle was full, tense, and bulging, and measured approximately 3 by 3 cm. The occiput was prominent. The pupils were equal but failed to react to light. There was convulsive blinking of the lids and unsustained lateral nystagmus of the eyes. There was no demonstrable nuchal spasm or rigidity. The lungs were aerated and no abnormal adventitious sounds audible. The respiratory rate was rapid, and the cardiac sounds were distant and feeble. The liver and spleen were not enlarged. No rose spots or petechiae were noted. All four extremities were cold and moderately cyanotic. Neurological examination revealed hyperactive slightly spastic patellar and Achilles tendon reflexes and bilateral ankle clonus. The Moro reflex was absent. Chvostek and Kernig signs were negative.

Hospital Course.—Lumbar puncture was performed, yielding 8 cc. of thick sanguinopurulent fluid which dripped fairly freely, suggesting increased cerebrospinal fluid pressure. The stylette was replaced, leaving the needle in the subarachnoid space while a Gram stain of the centrifuged sediment was being done. Meanwhile, a 23-gauge needle on polyethylene tubing was fixed in a scalp vein, and blood was obtained for type, Rh, cross match, and culture, followed by infusion of normal saline, approximately 50 cc., and 1 cc. of aqueous adrenocortical extract (Eschatin) and 7 mg. of secobarbital sodium were given into the tubing intravenously; the convulsion subsided, and her color and appearance seemed improved.

The initial laboratory findings were as follows:

Blood	
Red blood cells	4,620,000
Hemoglobin (gm./100 cc.)	13.5
White blood cells	13,200
Stab forms (%)	11
Segmented forms (%)	35
Lymphocytes (%)	50
Monocytes (%)	4
Cerebrospinal Fluid	
Red blood cells	48,000
White blood cells	44,500
Segmented forms (%)	100
Protein (mg./100 cc.)	750
Sugar (mg./100 cc.)	1
Smear	Many Gram-negative rods larger than H. influenzae

A coliform, Proteus, Salmonella, or Klebsiella, and, less likely, H. influenzae, infection was suspected, and since she had been treated recently with small doses of penicillin, dihydrostreptomycin and orally administered chlortetracycline, it was felt that all routes of therapy available should be utilized, as well as larger doses. At the initial spinal tap, 10 mg. of streptomycin and 10,000 units of penicillin in 5 cc. isotonic saline were injected intrathecally. Throat and anal swab cultures were taken. Chlortetracycline hydrochloride, 100 mg. in 200 cc. 5% dextrose in water was given intravenously at 10 to 15 drops per minute, followed by 50 cc. of whole blood, and a continuous intravenous of a mixture of three parts 10% dextrose in water to one part of Darrow's solution with added vitamins of the B complex, C, and K was maintained to give the patient a total intravenous intake of 200 cc. per kilogram of body weight the first 24 hours (600 cc.), and 150 to 200 cc. per kilogram every 24 hours thereafter. She received 100 mg. of chlortetracycline intravenously every 12 hours for four injections and was also given 100 mg. of streptomycin and 50,000 units of penicillin intramuscularly every three hours and 150 mg. per kilogram of body weight of sulfadiazine sodium every 24 hours subcutaneously in a 5% solution in four divided doses. The sulfadiazine therapy was stopped after 48 hours.

In an effort to combat an impending Waterhouse-Friderichsen syndrome, after the intravenous injection of 1 cc. of aqueous adrenocortical extract, she was given 1 cc. of lipoadrenal cortex intramuscularly every 12 hours for 48 hours (four doses).

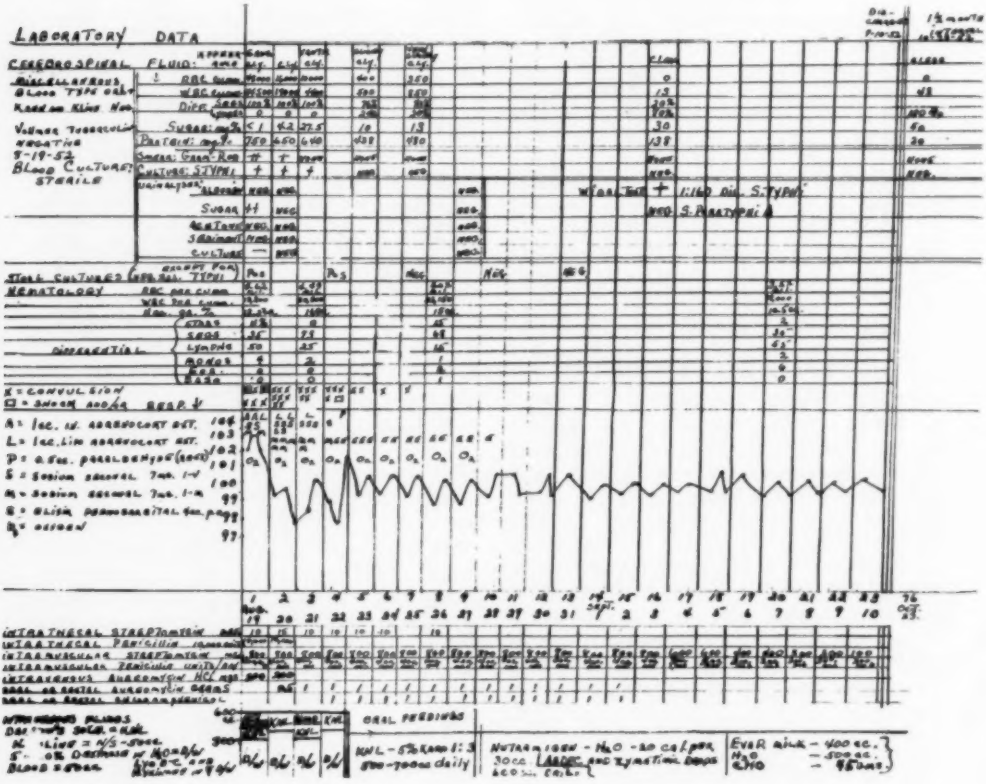
She was kept in an oxygen tent, with constant attendance at the bedside. Convulsions occurred repeatedly, but with diminishing intensity, over the next four days and were controlled by intravenous administration of 7 to 15 mg. of secobarbital sodium, with the same dose being given intramuscularly. On her third hospital day, her respiration became slow and her color cyanotic following an intravenous injection of 7 mg. of secobarbital sodium, and it was necessary to give her artificial respiration for 30 minutes and 0.25 cc. of caffeine-sodium benzoate intramuscularly. Subsequently, the convulsions became less intense and were controlled by administration of 0.5 cc. of paraldehyde in 20 cc. of olive oil by rectum on one occasion and 4 cc. of elixir of phenobarbital (15 mg. orally) three times a day, two times a day, then eliminated on Aug. 26, the seventh day.

A second blood transfusion was given on Aug. 21, 36 hours after the first. It was necessary to change scalp veins after each chlortetracycline injection because of an impending phlebitis. No

vein, however, became thrombosed. On the second day she seemed improved. Fifteen milligrams of streptomycin with 10,000 units of penicillin was given intrathecally after the removal of purulent spinal fluid, 12 hours after the initial tap.

On the third day, in vitro sensitivity tests of the organism recovered from the original spinal fluid revealed that chlortetracycline and streptomycin yielded the greatest zone of inhibition (12 mm.) and oxytetracycline (Terramycin) to less extent (10 mm.). Chloramphenicol was

After the sixth hospital day, she appeared to be out of danger and made a fairly rapid recovery. Oral feedings of 3 parts 5% Karo water to 1 part Darrow's solution were begun on the third day and standard Nutramigen (hypoallergenic food) formula (20 calories per 30 cc.) on the fifth day. She was also given Abdec (vitamins A, D, B_1, B_2, B_6, sodium panthenate, nicotinamide, and C) and Zymatinic drops (liver concentrate, ferrous gluconate, riboflavin [B_2, G], thiamine hydrochloride [B_1], pyridoxine nicotinamide, folic



not effective, nor were penicillin and sulfadiazine. Administration of the latter was stopped; penicillin was continued by intramuscular administration. After two days of intravenously administered chlortetracycline, the patient had begun to take oral feedings, so oral administration of 250 mg. of chlortetracycline every six hours was started; chloramphenicol therapy was begun on Aug. 22, when the organism was definitely identified as S. typhosa, since in vitro sensitivities are not always infallible.

acid, and alcohol). She had a few loose stools after her stool culture had become negative for pathogens, while taking chlortetracycline and chloramphenicol orally. These drugs were probably responsible. She received six intrathecal injections of streptomycin of 10, 15, and then 10 mg. each thereafter. The first two injections were given at 12-hour intervals, the next three at 24-hour intervals, and the last injection after 48-hours. The first three spinal fluid specimens yielded pure cultures of S. typhosa, after which the remaining three were

sterile, as well as the final tap eight days later. The blood culture was sterile, but two stool cultures were positive for S. typhosa on Aug. 19 and Aug. 22, the fourth day, after which three on alternate days were negative. Stool cultures of the parents were negative. On Sept. 4, the 16th day, the Widal test of the patient's blood was three+ in 1:20 to 1:80, 1+ in 1:160 dilution, and negative in 1:320. The control was negative, and there was no agglutination in any dilution against S. paratyphi A. No Widal test was run on the parents because they had had typhoid immunizations. Other laboratory findings including subsequent cerebrospinal fluid findings are included in the accompanying chart.

Bilateral subdural taps were performed on Aug. 25, the sixth day, with negative results. At the final lumbar puncture on Sept. 3, the 15th day, eight days after the last intrathecal streptomycin injection, the spinal fluid was crystal clear, the red blood cell count 0, the white blood cell count 13, lymphocytes 80%, segmented cells 20%, protein 138 mg. per 100 cc., sugar 30 mg. per 100 cc., and the smear and culture negative.

She received 250 mg. of chlortetracycline and chloramphenicol by oral or rectal administration every six hours until Sept. 3, the 15th day, when it was stopped because of vomiting and loose stools, after which the vomiting ceased and the stools became firm. Intramuscular administration of 100 mg. of streptomycin every three hours was given until Aug. 4, then reduced to every four hours until Aug. 6, every six hours until Aug. 8, then every eight hours, and it was discontinued on Aug. 10. Intramuscular administration of penicillin was continued until discharge, using 200,000 units of penicillin S-R daily after Aug. 3.

Upon discharge, on Aug. 10, twenty-three days after admission, she appeared normal in every respect and was seen in the office two weeks later, at which time no abnormal neurological findings were noted, the fontanelle was soft, and fundoscopic examination was negative. Her weight was 4000 gm., a gain of 1000 gm. since admission 34 days before. Further follow-up examinations and developmental assays will be done and electroencephalography and air studies, if indicated.

COMMENT

Typhoid and meningitis in the newborn infant may be very misleading. This child had few gastrointestinal symptoms, no petechiae, and no nuchal spasm. The disease apparently was ushered in with an upper respiratory infection or pneumonia, either of which may be a frequent finding in typhoid fever. Improvement occurred with therapy, then, when treatment was stopped, a fulminating infection recurred, rapidly progressing to meningitis with convulsions and collapse. This is also a proved case of Salmonella typhosa infection in which in vitro tests indicated chloramphenicol to be ineffective. Ripy's[4] 13-month-old child failed to respond to Chloromycetin, but recovered promptly when chlortetracycline (Aureomycin) was added. Our patient was given chlortetracycline intravenously at first, then orally, and intrathecal and intramuscular administration of streptomycin; both chlortetracycline and streptomycin fortunately proved the most effective by sensitivity studies. Chloramphenicol therapy was started after the patient was well on the way to recovery, and it is felt that it did not contribute to the favorable outcome.

A summary of the bacteriological and serological characteristics of the organism isolated both from the cerebrospinal fluid and the feces, pointing conclusively to its correct identity as S. typhosa follows.

A smear of the centrifuged fluid was made and many Gram-negative pleomorphic rods were seen; the remaining sediment was inoculated into tryptose phosphate broth and fluid thioglycolate medium. After less than 18 hours incubation, a heavy growth was evident. A suspension from this showed motile rods and Gram stain again showed Gram-negative rods.

The lactose fermentation tube, desoxycholate agar plate, Levine eosine-methylene blue agar, and Difco SS agar were streaked, and pure culture of typical Salmonella colonies appeared. The lactose fermentation tube showed no change, the desoxycholate plate had no growth. Kligler's sugar-iron-agar slant was inoculated, and the tube showed alkaline slant, acid butt with formation of hydrogen sulfide, and no gas. From the Kliger's sugar-iron-agar slant, urea broth, and fermentation tubes of xylose, dextrose, maltose, saccharose, lactose, rhamnose, mannitol, dulcitol, and salicin were inoculated. The urea was not hydrolyzed, and the sugars again showed typical S. typhosa reaction.

Salmonella polyvalent antisera agglutinated the organism, and somatic antigen serum IX with flagellar factor d showed strong agglutination.

A rectal swab placed in Selenite F enrichment broth was streaked immediately on SS agar, eosine-methylene blue agar plate, and after 18 hours'

incubation a pure culture was obtained. Similar steps were followed as on the colonies isolated from the cerebrospinal fluid.

SUMMARY

A case believed to be that of the youngest surviving patient in the literature with Salmonella typhosa meningitis is reported. Growth of the organism in vitro was inhibited by chlortetracycline (Aureomycin) and streptomycin equally well, to a less extent by oxytetracycline (Terramycin), and not at all by chloramphenicol, penicillin, or sulfadiazine.

Dr. J. F. Pilcher and Andrew Minarik, M. T., did the bacteriological studies and Dr. William A. Ewert referred this case.

REFERENCES

1. Tupas, A. V., and Quintos, F. N.: Typhoid Fever in Children, J. Phillipine M. A. **16**:545, 1936.

2. Adams, S. S.: A Study of 337 Cases of Enteric Fever in Children, Arch. Pediat. **21**:81, 1904.

3. Griffith, J. P. C.: Typhoid Fever in Infancy: An Analysis of 75 Cases, Arch. Pediat. **29**:565, 1912.

4. Ripy, H. W.: Typhoid Fever in an Infant Complicated by Typhoid Meningitis: Therapeutic Failure with Chloromycetin; but Response to Aureomycin, J. Pediat. **36**:376, 1950.

5. Kantor, H. L.: Salmonella Bredeney Meningitis: Case Report of a 19 Day Old Infant, Pediatrics **9**:597, 1952.

6. Henderson, L. L.: Salmonella Meningitis: Report of 3 Cases and Review of 144 Cases from the Literature, Am. J. Dis. Child. **75**:35k, 1948.

7. Beene, M. L.; Hansen, A. E., and Fulton, McD.: Salmonella Meningitis: Recovery from Meningitis Due to Salmonella Sp. (Type Montevideo), with Consideration of the Problem of Salmonella Meningitis, A. M. A. Am. J. Dis. Child. **82**:567, 1951.

News and Comment

ANNOUNCEMENTS

Course in Neuromuscular Diseases of Children, Cook County Graduate School of Medicine.—The Cook County Graduate School of Medicine announces a two-week intensive course in Neuromuscular Diseases of Children, with special emphasis on cerebral palsy, to be given by Dr. Meyer A. Perlstein for the two-week period of June 18 to 29. This is an intensive, didactic, and clinical course designed for pediatricians, orthopedists, neurologists, and physiatrists interested in the care and treatment of children with neuromuscular handicaps. Emphasis will be placed on the practical clinical aspects of treatment and rehabilitation procedures. The course will include several field trips to demonstration clinics and treatment centers. The fee for the course, which is $225, includes the cost of luncheons as well as the expense of travels, meals, and accommodations on the various trips. Registration in the course is limited. For further information, write to John W. Neal, Registrar, Cook County Graduate School of Medicine, 707 S. Wood St., Chicago.

Fellowship in Pediatric Renal Research.—A fellowship in renal research will be available beginning July 1, 1956, in the Department of Pediatrics, Western Reserve University School of Medicine, Cleveland. The candidate would be expected to spend approximately two-thirds of his time in laboratory research and one-third in clinical work with patients under investigation. Salary: $4500 to $5000. Applicants with minimum training of two years in pediatrics preferred. Direct correspondence to Walter Heymann, M.D., 2103 Adelbert Road, Cleveland 6.

Spring Clinics.—The Valley Children's Hospital and Guidance Clinic, Fresno, Calif., will hold its second Annual Spring Clinics April 27 and 28, 1956. The registration fee is $15 for the two-day session.

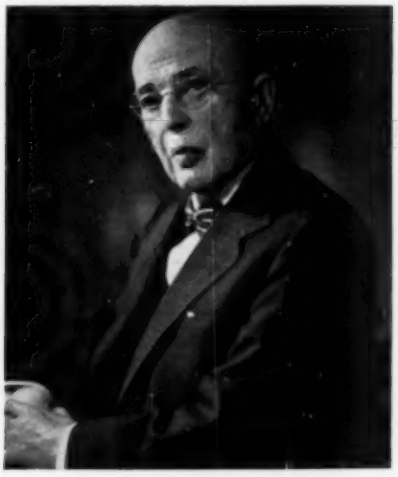
The guest speakers will be Dr. Horace L. Hodes, of New York, and Dr. Edward B. D. Neuhauser, of Boston.

Obituaries

ISAAC ARTHUR ABT, M.D.
1867-1955

Isaac Arthur Abt was born at Wilmington, Ill., the son of Levi and Henrietta, on the 18th day of December, 1867. He was married in 1897 to Lina Rosenberg and had two children, Arthur E. and Lawrence E.

Dr. Abt completed his first two years in medicine in 1889, at the Johns Hopkins University. He then continued his medical education and graduated from the Chicago Medical College (Northwestern University Medical School) in 1891. He served an internship at the Michael Reese Hospital, in Chicago, from 1891 to



ISAAC ARTHUR ABT, M.D.
1867-1955

1893, and continued his medical education with a postgraduate course at Vienna and Berlin from 1893 to 1894. From 1897 to 1901 he was Professor of Diseases of Children at Northwestern Women's Medical College.

He became Associate Professor of Pediatrics at Rush Medical College in 1892 and served until 1908. In 1909 he became Professor of Pediatrics at Northwestern University Medical School, which position he held until 1942. He was named Emeritus Professor of Pediatrics in 1942, which title he held until his death. He was consulting physician to the Children's Memorial Hospital, Sarah Morris Hospital, and St. Luke's Hospital. He was also attending pediatrician at Passavant Hospital, in Chicago.

Dr. Abt was largely responsible for the founding of the Sarah Morris Children's Hospital, which is in close affiliation with the Michael Reese Hospital.

He was Honorary Member of the Minnesota Chapter of the Alpha Omega Alpha, being elected a member. He was made Chevalier of the Legion of Honor and received the degree of D.Sc. from Northwestern University.

Dr. Abt published many scientific papers; most, if not all, were devoted to treatises or discussions on pediatric conditions. He was also the author of two books, "The Baby's Food," published in 1917, and the "Baby's Doctor," published in 1944. Probably his most eminent contribution in this line was as Editor of "Abt's System of Pediatrics."

Dr. Abt was President of the American Pediatric Society in 1926. He was a member of the American Medical Association. He also was a member of the American Academy of Pediatrics and was President in 1930.

In his younger days, Dr. Abt was a regular attending man at the Cook County Hospital, where many of the younger men learned to know and appreciate him. He was willing to discuss cases and gave us all a broader view of the subject. Dr. Abt was essentially a student. He spent long hours in his library when he was not busy seeing patients and oftentimes would study there until the small hours of the morning, and then get up early for a busy day. His knowledge of pediatrics was broad and deep, and it showed in his teaching and practice. He was always kind and considerate, but not by any means easygoing when principles were concerned.

Dr. Abt died on Nov. 22, 1955, of coronary thrombosis preceded by a malignancy of the tongue. We have lost a great deal in the going of this genial companion, and the world has been better because of his life. He was a source of inspiration to younger men and gave much of his busy life in instructing them. He was much interested in public health activities and long an active member of the Infant Welfare Society of Chicago. His was indeed a full and noble life filled with kindness and usefulness.

C. G. GRULEE, M.D.

Abstracts from Current Literature

Prematurity and Congenital Deformities

GREIG'S HYPERTELORISM AND ITS RELATION TO THE SYNDROMES OF CRANIAL AND FACIAL DYSOSTOSIS. C. ZUNIN, Minerva pediat. **7**:71 (Jan. 27) 1955.

The cases of two children with the hypertelorism of Greig are reported; one of the children had a supernumerary thumb. The syndrome appears to be a definite clinical entity, and its etiology is probably similar to that found in premature closure of the cranial sutures, as in brady-cephaly, in many cases of which there is hypertelorism.

HIGGINS, Boston.

HYPOPLASIA OF THE MUSCLES OF THE ABDOMINAL WALL. D. BULLIO, Minerva pediat. **7**:80 (Jan. 27) 1955.

A 17-day-old infant had hypoplasia of the muscles of the abdominal wall; the skin over the abdomen is described as feeling and looking like orange peel. The baby did have a long and large colon, but the functioning of the intestinal tract was normal. The etiological possibilities of this condition are discussed, but no definite conclusion was reached.

HIGGINS, Boston.

DEVELOPMENT AND MORBIDITY OF PREMATURE INFANTS IN HOME CARE UNDER SUPERVISION OF HEALTH VISITORS. ELKJAER LAURSEN and J. FLAMAND CHRISTENSEN, Ugesk. læger **116**:683 (May 6) 1954.

The authors report on 288 premature infants (4 infants of 1001-1500 gm. birth weight, 45 of 1501-2000 gm., and 239 of 2001-2500 gm.) nursed at home under supervision of health visitors. The nutrition, the gain in weight, the development, and the morbidity of these infants and of a comparable group of infants with normal birth weight was studied. The duration of breast-feeding was slightly less for the premature infants. At the age of 6 months, 29% of the premature infants were breast-fed or received mixed feeding, while the corresponding figure was 33% for full-term infants. The gain in weight of premature infants was slightly less during the first months, but subsequently it was equal to or even better than that of infants of normal birth weight. The gain in weight was independent of the form of nutrition or of the housing conditions. By the end of the first year the somatic and static development was only slightly retarded. The morbidity was the same for premature and mature infants, but the course taken by the diseases was severer among the premature infants. The morbidity was twice as high in infants fed on cow's milk as in breast-fed infants and similarly twice as high in infants living in poor housing conditions as in infants with good housing conditions.

WALLGREN, Stockholm.

Newborn

NEONATAL DEATH—ITS PREVENTION. FREDERICK H. FALLS, Illinois M. J. **105**:239-242 (May) 1954.

Falls believes that the obstetrician has the responsibility for attempting to prevent certain prenatal and postnatal deaths because of conditions which develop during early pregnancy, after the period of viability, during labor, and immediately following its conclusion. The crucial diagnostic and therapeutic problems evolved and the associated hazards and dangers which present themselves in certain conditions are discussed. Among these conditions are cephalopelvic disproportion, premature labor, breech presentation, placenta previa, villamentous insertion of cord, threatened rupture of the uterus, twins, eclamptogenic toxemia, and fibroid uterus.

BARBOUR, Peoria, Ill.

THE PATHOLOGY OF NEONATAL DEATH. JOSEPH D. BOGGS, Illinois M. J. **105**:248-250 (May) 1954.

Boggs points out that in the 1944 records of the United States Bureau of Vital Statistics 86% of all deaths among premature infants fall into the classification of prenatal and natal causes.

In the discussion which follows, anoxia is given as the most frequent cause of death in the neonatal period. Anoxia is the most frequent cause of death before birth, during labor, and in the neonatal period. General factors commonly precipitating anoxia are lowering of the oxygen in the placental circulation, alteration of sensitivity of the infant's respiratory center, reduction of the oxygen-bearing blood to the infant, and reduction of the CO_2-O_2 exchange within the infant's lungs.

Different cells have different responses to anoxia; therefore certain values in the serum, particularly electrolytes and pH, may not adequately evaluate the electrolytes and pH of a particular cell type in a particular organ. The human organism in the newborn is physiologically and anatomically immature. Minor alterations as seen by the pathologist assume a much greater importance than if they are seen in later life. Severe damages may occur with a long-standing relative anoxemia.

Congenital cardiac anomalies have anoxia as a mechanism, producing irreversible changes and death. In babies delivered by Caesarean section, large amounts of aspirated fluids are often found in the lungs, and the loss of blood may contribute to an anoxia.

Intracranial hemorrhage is not infrequently found by the pathologist in the newborn period. The abdominal viscera may be damaged by trauma at birth and cause death. Tracheoesophageal fistulae and related anomalies of the esophagus should be mentioned, as should be blood-Rh-factor incompatibilities.

BARBOUR, Peoria, Ill.

THE NORMAL NEWBORN AND THE ANENCEPHALIC: REFLECTIVITY, REACTIVITY, AUTOMATISMS. ANDRE-THOMAS, Presse méd., Suppl. 42, p. 885 (June 9) 1954.

A case of protuberantial anencephalus is reported, and the reactions are studied in comparison with those of a normal newborn infant. It presents similar findings as regards the movements in the whole, particularly those of erecting the body and those rather localized of the hand and fingers.

There are in protuberantial anencephalus some osteotendinous reflexes similar to those from the adult, which are not to be found in the normal newborn infant, the fact being explained by the presence of tonicity in flexion of the upper limbs in the normal newborn infant.

The reflex of incurvation of the trunk is present and even exaggerated, as are some reflexes observed in other types of anencephalus and presumably due to liberation phenomena.

This case of protuberantial anencephalus was also remarkable by its uttering a sort of babbling and warbling, which is usually to be only heard from older infants.

Finally it was possible, through some localized stimulations, to start epileptiform jerks in the lower limb, which phenomenon is classed by the author among those of "repercussivity."

FROM THE AUTHOR'S SUMMARY.

THE ACTIVITY OF THE SERUM PROTHROMBIN CONVERSION ACCELERATOR' (OR FACTOR VII) IN THE BLOOD OF THE NEWBORN. F. VECCHIO and V. BAFFI, Pediatria **62**:153 (March) 1954.

The method of Koller, as modified by the authors, was used to compare the activity of Factor VII in the blood from the umbilical cord of the newborn infant and in adult blood. This activity was found to be much lower in the umbilical cord blood.

HIGGINS, Boston.

THE INFANT MORTALITY IN BREECH PRESENTATION. FOLKE RØNNIKE, Nord. med. **51**:331 (March 4) 1954.

The author compares two series of breech deliveries, one Swedish, that was purely clinical in that almost no birth occurred outside the maternity hospitals, and one series of nonclinical cases from Denmark, comprising births in Odense's environments. The mortality rate found is regarded as the minimal figure for a nonclinical series, since only cases of pathological childbirth are admitted to the Danish obstetric departments. The neonatal mortality in the nonclinical group was based largely in the birth and death records. The mortality rate in the nonclinical cases was 9.11% for children with a birth weight of 2500 gm. or more and 9.38% for children with a birth weight of 2000 gm. In the clinical cases the figures were 3.51% and 4.22% respectively. These figures, the author maintains, argue in favor of hospitalization of breech deliveries.

WALLGREN, Stockholm.

ASPHYXIA, SHOCK, AND GASTROINTESTINAL OXYGEN THERAPY IN THE NEWBORN INFANT. Y. ÅKERRÉN, Nord. med. **52**:1759 (Dec. 16) 1954.

Asphyxia and shock are two closely associated conditions. Clinical and anatomical findings suggest that conditions attending shock are very common in newborn infants dying with symptoms of asphyxia. Usually the anatomical changes are especially pronounced in the liver. With regard to the apparently major role in shock of liver anoxia and related disturbances of the liver function, the theoretical premises are discussed for adequate treatment of asphyxia and shock in the newborn infant. Due to the favored position of the liver from the standpoint of oxygenation during intrauterine life, neonatal asphyxia is accompanied by fulminant liver anoxia. Gastrointestinal oxygen therapy, which serves primarily to increase the oxygen content of the portal blood, should therefore be of value with regard the shock factor. Methods are discussed and recommended in which the placental blood is utilized for autotransfusion in the asphyctic newborn.

WALLGREN, Stockholm.

TOXIC SYMPTOMS CAUSED BY THERAPEUTIC DOSE OF NICETAMIDE AND CARDIAZOL IN NEWBORN INFANTS. P. W. BRESTRUP, Ugesk. læger **116**:1046 (July 15) 1954.

Six newborn infants developed toxic symptoms with convulsions following the administration of large therapeutic doses of niketamide (Coramine) and Cardiozol. As the clinical effect of these therapeutics is doubtful and toxic doses too easily reached, their use in newborn children should be abandoned.

WALLGREN, Stockholm.

Acute Contagious Diseases

THE PROPHYLACTIC EFFICACY OF GAMMA-GLOBULIN IN ACUTE POLIOMYELITIS AND IN VARICELLA. U. SALA, Lattante **25**:737 (Nov.) 1954.

A 6-month-old child in a foundling institution developed acute poliomyelitis. At about the same time, a boy inmate came down with whooping cough. Both patients were isolated as soon as the diagnosis was made. As a prophylactic measure, all the 100 children and 40 mothers were given injections of γ-globulin. Within one week, another child developed chicken pox.

There were no other cases of either whooping cough or of poliomyelitis in the institution, but practically every child and mother who had not previously had chickenpox developed the disease.

HIGGINS, Boston.

DIPHTHERITIC LARYNGITIS. JULIO MENEGHELLO RIVERA, OSCAR UNDURRAGA, and HAYDEE SEPULVEDA, Rev. chilena pediat. **25**:159 (April) 1954.

The experience presented that obtained in 79 patients with diphtheric laryngitis observed in the Contagious Service of the Manuel Arriaran Hospital during a period of seven years (1946-1952). The disease appeared most often in patients above 3 years of age (58.2%) and in autumn and winter (76.9%). In the majority of the cases the onset was slow, but in 36.7% the initiation was sudden. Besides the respiratory obstruction of different intensity, symptoms of toxemia were present in 78.4%. The diagnosis of diphtheric laryngitis is presented before a laryngeal obstruction, but the endoscopic and bacteriological examination of the secretions are the surest means for formulating a reliable diagnosis. Besides antitoxin, which was received by all the patients, and the antibiotics, especially penicillin, intubation was performed in the 48.6% of the patients and tracheotomy in 16.4%. Transient sequels, such as disphonia or alphonia or paresia or paralysis of the vocal cords were observed on six occasions. The mortality amounted to 17 cases (21.5%) and the corrected mortality, leaving out 9 patients who died before 24 hours of hospitalization, was 11.2%. Thirty-eight patients were intubated, of which 5 died and 13 were tracheotomized (of this number 8 died). The anatomopathological findings revealed descending diphtheria in 9 patients, bronchopneumonia in 11, and atelectasis in 3.

FROM THE AUTHORS' SUMMARY.

Acute Infectious Diseases

A STUDY OF ILLNESS IN A GROUP OF CLEVELAND FAMILIES: VIII. RELATION OF TONSILLECTOMY TO INCIDENCE OF COMMON RESPIRATORY DISEASES IN CHILDREN. LOIS P. MCCORKLE, RICHARD G. HODGES, GEORGE F. BADGER, JOHN H. DINGLE, and WILLIAMS S. JORDAN JR., New England J. Med. **252**:1066 (June 23) 1955.

The authors observed 230 children over a four-year period and tabulated the incidence of the common respiratory diseases. The results of their studies are expressed as incidence rates of the

common respiratory diseases among children who had tonsillectomies and among those who did not. Presumably, adenoidectomy was not done simultaneously.

Attack rates for the common respiratory diseases among children who had had a tonsillectomy were very similar to those among children who had not had this operation. There was no indication of a difference in type of common respiratory diseases between the two groups of children.

The 26 children who had a tonsillectomy while under observation were found to have had a higher than expected rate of common respiratory disease both before and after operation. Tonsillectomy did not materially alter this incidence.

WHEELOCK, Washington, D. C.

CLINICAL AND MICROBIOLOGIC ASPECTS OF SALMONELLOSIS. GEORGE M. EISENBERG, ANTHONY J. PALAZZOLO, and HARRISON F. FLIPPIN, New England J. Med. **253**:90 (July 21) 1955.

The authors suggest that the occurrence of human infection with Salmonella organisms (other than typhoid) is more important than is generally recognized.

Three main clinical syndromes are listed: gastroenterocolitis, which can cause symptoms ranging from mild diarrhea to a cholera-like picture; bacteremia or septicemia, either with or without extraintestinal localization in meningeal, renal, pulmonary, pleural, and similar sites; a clinical picture similar to but usually milder than that seen in the typical case of typhoid fever; carriers, either convalescent or asymptomatic.

Emphasis is placed on the problem of diagnosis, since many Salmonella of etiologic significance may be missed by conventional serodiagnostic techniques.

Ninety-five proved cases of salmonellosis (55 adults and 40 children) were analyzed and the findings summarized. Of this number six adults and two children succumbed to an infection whose protean character may puzzle the physician sufficiently to distract him from a diagnosis and hence prompt antimicrobial treatment.

WHEELOCK, Washington, D. C.

TREATMENT OF TUBERCULOUS MENINGITIS WITH TUBERCULOSTATIC DRUGS IN COMBINATION WITH CORTISONE. F. MICHEL and W. PULVER, Schweiz. med. Wchnschr. **85**:717-721 (July 23) 1955.

Treatment of eight cases of the meningitis with cortisone in combination with streptomycin, dihydrostreptomycin, Rimifon, and at times *p*-aminosalicylic acid, are reported. The age of four of the eight cases was below 12 years. The time elapsed since initiation of treatment varied from 3½ to 15 months. The results up to that time were very good.

AMBERG, Rochester, Minn.

HYDROCORTISONE IN THE TREATMENT OF ORCHITIS DUE TO MUMPS. L. MARTONI, Clin. pediat. **37**:403 (June) 1955.

Hydrocortisone, 125 mg. the first day, 100 mg. the second day, 75 mg. the third day, and 50 mg. the fourth day given orally was used in the treatment of three cases of mumps orchitis. The therapeutic results were excellent, with relief of pain and disappearance of the fever in from 12 to 24 hours. The swelling and tenderness of the testicles had receded completely by the end of the second day; examination 20 to 25 days later revealed no atrophy.

One of the patients had mumps encephalitis, starting one day after the onset of the parotitis; the fever and symptoms had subsided five days later, but two days after that, the fever again rose, with abdominal pain, diarrhea, and orchitis. A diagnosis of pancreatitis as well as orchitis was made. The hydrocortisone relieved the pancreatitis as well as the orchitis.

HIGGINS, Boston.

THE FEEDING OF POTASSIUM CHLORIDE AND ITS EFFECT ON THE POTASSIUM AND SODIUM BLOOD SERUM CURVES IN CHILDREN WITH POLIOMYELITIS. C. ACETO, Clin. pediat. **37**:407 (June) 1955.

Observations were made on 14 children with poliomyelitis to which 0.05 gm. per kilogram of KCl was given by mouth 12 hours after the last feeding. The K and Na contents of the blood sera were determined hourly for four hours. The same determinations were repeated (1) when desoxycorticosterone and (2) epinephrine were given in addition to the KCl. The results showed that the K and Na metabolism of children with poliomyelitis did not deviate from that of normal children.

HIGGINS, Boston.

CLINICAL OBSERVATIONS AS TO THE EFFECT OF MEASLES ON THE CLINICAL COURSE OF TUBERCULOSIS. B. CARLETTI, Minerva pediat. **7**:51 (Jan. 27) 1955.

The cases of 121 children who had had measles within 12 months before admission to the hospital with tuberculosis and of 105 children who contracted measles while undergoing hospital treatment for tuberculosis are analyzed and compared to the cases of tuberculosis in children who had not had measles during the year before admission or while hospital patients.

The children who had recently had measles were more prone to have tuberculous bronchopneumonia or miliary tuberculosis and less likely to have pleurisy, meningitis, or calcified hilar glands or pulmonary foci. The child who has had or has measles tends to require a longer hospital stay if the tuberculous involvement is pulmonary but not if miliary or meningeal.

Hospital-contracted measles definitely prolonged the course of treatment of most of the tuberculous children. The measles in the hospital-contracted cases was usually relatively mild.

HIGGINS, Boston.

NEUROPSYCHIATRIC DISTURBANCES FROM CHLORAMPHENICOL IN THE COURSE OF PARATYPHOID B FEVER. E. SEGAGNI, Minerva pediat. **7**:219 (Feb. 24) 1955.

A 4-year-old girl was admitted to the hospital after eight days of illness with fever, drowsiness and diarrhea. A diagnosis of paratyphoid B fever was established three days later. Then chloramphenicol, 100 mg. per kilogram per day, was administered for 11 days (16.5 gm. in all). A roseola rash appeared on the second day of treatment and lasted for two days. The temperature fell to normal on the fifth day of treatment, and there were no more vomiting attacks or loose stools after the sixth day. From the third day, the child was described as calm, sleeping well, and interested in her surroundings; but on the eighth day she became mentally confused and had hallucinations; she saw strange animals on the walls of her room; she did not recognize her nurses. The symptoms were more marked at night. After three days the symptoms had disappeared. The chloramphenicol therapy had been given throughout the stage of the mental disturbance. Since the neuropsychiatric symptoms had occurred after the fever had receded and the infection resolved, the belief is expressed that they were due to the toxic action of the antibiotic drug.

HIGGINS, Boston.

THE PROPHYLACTIC USE OF GAMMA-GLOBULIN AGAINST MEASLES. M. MALASPINA and E. SEGAGNI, Minerva pediat. **7**:503 (April 21) 1955.

Thirty-four hospitalized infants, sick with various diseases, were given prophylactic injections of γ-globulin following their exposure to measles. Of 26 infants receiving injections within five days after exposure, three developed measles and eight an attenuated measles. Of eight infants receiving injections on the 6th to 10th days after exposure, five developed measles and two an attenuated measles. None of the infants who developed typical measles were critically ill, nor were there any complications.

HIGGINS, Boston.

RESPIRATORY DISTURBANCES DURING THE COURSE OF POLIOMYELITIS: TWO CASES OF PULMONARY ATELECTASIS. S. SCARABICCHI, Minerva pediat. **7**:542 (April 28) 1955.

Two cases of poliomyelitis are reported in which atelectasis on one lung had occurred; one patient died, having the bulbar type; the other patient recovered from this episode, although still having considerable paralysis of the respiratory muscles. The author discusses the possible therapeutic measures available to combat such disturbing complications of poliomyelitis as pulmonary edema, laryngeal paralysis, mucous obstruction of the airways, paralyzed respiratory muscles, and disturbances of the respiratory center.

HIGGINS, Boston.

THE USE OF ERYTHROMYCIN IN PEDIATRICS. W. KARPINSKI, Wien. klin. Wchnschr. **67**:515-516 (July 15) 1955.

Erythromycin was given to a number of children with bronchopneumonia, laryngitis, pertussis pneumonia, staphylococcic emphysema, and sepsis with beneficial results. All patients were penicillin-resistant.

AMBERG, Rochester, Minn.

MEASLES ENCEPHALITIS. JENS STEEN, Nord. med. **52**:1468 (Oct. 21) 1954.

The author reports on 21 cases of measles encephalitis, referable to an 18-year period. No rising incidence of this complication could be found. The mortality rate was 32.8%. Four of the five patients who died were girls. In three other publications the same high mortality rate among girls has been noted. In Norway, 50% more girls than boys died of measles in the last five years. All patients who died had previously suffered from diseases which might have affected the central nervous system. Follow-up study of the surviving children showed that 30% had completely recovered, 15% had mild sequelae, and 30% serious sequelae. Of the six patients wih serious sequelae, two had mental defects, one had severe spastic palsy, one had mild palsy, and the remaining two had epilepsy. WALLGREN, Stockholm.

STAPHYLOCOCCAL INFECTION RESISTANT TO ANTIBIOTICS. PER HEDLUND, Nord. med. **52**:1471 (Oct. 21) 1954.

Five cases of infections were caused by Staphylococcus aureus. A boy 13 years old died of frontal sinusitis and leptomeningitis. Two women, aged 31 and 54 years, respectively, suffered from acute pneumonia and died. An 8-year-old girl with severe pansinusitis and a woman, aged 38, with sepsis survived. The increased resistance of Staphylococci to antibiotics and treatment of infections caused by these micro-organisms are discussed. WALLGREN, Stockholm.

GENERAL CONTROL MEASURES AGAINST POLIOMYELITIS. SVEN GARD, Nord. med. **52**:1682 (Dec. 2) 1954.

Poliomyelitis is rapidly growing in importance. In the last 35 years the attack rate in Sweden shows an eightfold increase, due mainly to the involvement of ever older age groups. A characteristic feature of the epidemiology of the disease is the large proportion of subclinical or avirulent infections, which from immunological studies are estimated at about 350 for every clinically manifest case. Silent infections confer serological immunity and apparently good protection against invasion of the central nervous system. The risk of central nervous system involvement in primary infection is probably at least 10 times higher in adults than in infants. In infected individuals the virus is present in throat secretions for a comparatively short period of time but in the stools for many weeks or sometimes months. Disseminations of the virus may thus follow many different paths: by direct contact, by contaminated hands, by coprophagus flies, by contaminated food and water. This fact, together with the predominance of silent infections, makes the detection of sources and modes of infection in individual cases extremely difficult and quite impossible without the aid of the laboratory. Immunological surveys have shown that the level of immunity in the age groups of about 40 years and above is higher than might be expected on the present rate of acquisition of immunity in the ages below 20 years, indicating that exposure to infection was more intense at the turn of the century than it is today. The generations born since 1910 are therefore less thoroughly protected against paralytic attacks. Consequently, unless effective control measures are undertaken, we must expect further increase in attack rates in the future, primarily in the age groups above 40. General control measures include isolation or confinement of virus excreters, rigorous personal hygiene, improvement of the water and sewage sanitation, and fly abatement. Rational control is possible only through extensive cooperation between public health personnel on all levels and the laboratories. With the present inadequate resources the difficulties will be insurmountable in the midst of an epidemic. For the time being the most rational approach seems to be a concentration of the campaign upon the early sporadic cases and small outbreaks occurring in April or May. By doing so one might hope to quench an incipient epidemic. WALLGREN, Stockholm.

SUBDURAL EFFUSION IN PURULENT MENINGITIS. ODD GARBORG, Nord. Med. **52**:1762 (Dec. 16) 1954.

Out of 13 patients treated for purulent meningitis during the last one and one-half years at the University Pediatric Clinic in Oslo there were 3 in which subdural effusion was found. These three cases are presented in detail. It is reasonable to believe that with early diagnosis and adequate treatment subdural effusion can be a preventable sequela of purulent meningitis. The

first case was a baby boy 10 weeks old, with Staphylococcus aureus meningitis. A subdural tap was performed without effect, and he died at 3½ months of age. The second patient was a 7-week-old boy with meningitis due to hemolytic streptococci. By repeated subdural taps and antibiotic treatment the boy eventually could be discharged healthy. The third patient was a 4-month-old girl with purulent meningitis without demonstrable bacteria. Successful treatment was by subdural taps and antibiotics.

WALLGREN, Stockholm.

TREATMENT OF PSEUDOCROUP. GUNNAR NILSSON and INGEMAR OLOF, Svenska läk.-tidning. **51**:2487 (Oct. 1) 1954.

The authors report 392 cases of pseudocroup treated during a 28-month period. Six children were tracheotomized; no child died. The principles of the treatment were early admission to hospital in every case and antibiotics (penicillin, streptomycin, or Chloromycetin). When the symptoms have been severe, the antibiotic treatment has been combined with cortisone. The water balance has been controlled. If necessary tracheotomy should be performed before the child has been fatigued; after tracheotomy, desiccation of the respiratory tract should be prevented.

WALLGREN, Stockholm.

IS PRIMARY ATYPICAL PNEUMONIA RESISTANT TO THERAPY? ANDERS BERGLUND, Svenska läk.-tidning. **51**:3211 (Dec. 10) 1954.

The author reports 55 cases of virus pneumonia. It was not possible to show that cases that had been treated by different kinds of antibiotics and sulfonamides had shorter courses than untreated cases.

WALLGREN, Stockholm.

ANTIBIOTIC TREATMENT OF HEMOPHILUS INFLUENZAE MENINGITIS. C. MOSE, Ugesk. læger **116**:1069 (July 22) 1954.

This is a report of 31 children suffering from Hemophilus influenzae meningitis treated in the years 1932-1954. Twenty-five of the children were 3 years of age or less. Only one out of 10 cases survived of those treated with sulfonamides and penicillin. After the advent of streptomycin, this antibiotic was used usually combined with penicillin, sometimes with serum and for the last years with Chloromycetin or Terramycin. During this period only one of 21 children died. The mortality has thus fallen from 90% to 5%.

WALLGREN, Stockholm.

POLIOMYELITIS WITH PERSISTENT TOTAL EXTERNAL OPHTHALMOPLEGIA. HANS EHLERS, Ugesk. læger **116**:1731 (Dec. 9) 1954.

This is a report of a 4-year-old boy who fell severely ill with poliomyelitis with respiratory distress. A tracheotomy was performed. The spinal fluid contained more than 200 cells. After nine days it was observed that his eyes stood absolutely unmoveable. The eyelids could not be moved deliberately. The pupils were of the same size and reacted normally. Ophthalmoscopy showed nothing of significance. The boy could look at and grasp objects that were held in his line of vision, but he could not follow these objects with his eyes or by moving his head. If the object produced some noise he moved his head at this direction, but visual influence was not sufficient to produce a turning of his head. Purposely, without looking, he could move his head deliberately.

WALLGREN, Stockholm.

LABILITY OF SEROLOGIC TEST FOR INFECTIOUS MONONUCLEOSIS IN CHILDREN. T. BENNIKE, Ugesk. læger **116**:1784 (Dec. 23) 1954.

Forty-four unselected cases of infectious mononucleosis, of whom sixteen were under 15 years of age, were studied. Hitherto it was shown that children often have low serologic titers. In only four children was a Paul-Bunnell test of 1 : 128 or above found, while this titer was obtained in two-thirds of the adult cases. In children the titer often changes from positive to negative during the first month of the disease; while this occurred in 6 out of 16 children, it occurred only once in 28 adults.

WALLGREN, Stockholm.

Chronic Infectious Diseases

RECURRENT TUBERCULOUS MENINGITIS. ARCHIBALD L. HOYNE, J. H. DIAMOND, and ALLEN SCHULTZ, J. A. M. A. **155**:1234 (July 31) 1954.

A 15-year-old Negro girl had three recurrences of tuberculous meningitis. All were treated with streptomycin intramuscularly. (No intrathecal treatment was given.) She is now the mother of three children.

KIMBALL, Evanston, Ill.

EPIDEMIC HISTOPLASMOSIS AND AIRBORNE HISTOPLASMA CAPSULATUM. MARTHA J. IBACH, HOWARD W. LARSH, and MICHAEL L. FURCOLOW, Proc. Soc. Exper. Biol. & Med. **85**:72-74 (Jan.) 1954.

An entire farm family of five near Atchison, Kan., became ill with an influenza-like illness about 10 days after cleaning an unused chicken house. All had pulmonary lesions (x-ray), and all initially had a positive serological test for histoplasmosis, followed by falling titers. Histoplasma capsulatum was isolated from farm animals and from the soil inside and immediately outside the chicken house. A similar epidemiological picture was found near Beverly, Mo. The air in the chicken houses was sampled, using the Venturi Scrubber sampler. The samples were filtered and suspended in saline, the suspension containing penicillin and streptomycin, and injected intraperitoneally into white Swiss mice which were give penicillin subcutaneously. Four weeks after inoculation the mice were killed and macerated tissues (liver, spleen, adrenals) were cultured on brain heart infusion plate with 10% blood and Sabouraud's plates and incubated for four weeks. H. capsulatum was isolated twice from the Kansas and three times from the Missouri site. This study represents the first isolation of the fungus from the atmosphere.

HANSEN, Galveston, Texas.

THE TREATMENT OF TUBERCULOUS MENINGITIS WITH DIHYDROSTREPTOMYCIN AND ISONIAZID. FLORENCIO N. QUINTOS, TEODORA OCAMOP-VILLADOLID, and MAGDALENA B. ELICANO, Philippine J. Pediat. **3**:14-21 (Jan.-March) 1954.

This is a report of the results of the treatment of 35 cases of tuberculous meningitis in children with dihydrostreptomycin and isoniazid, with a recovery rate of 80%. The dosage and manner of administration are described. A few sample cases are mentioned.

FROM THE AUTHORS' SUMMARY.

THE PSYCHIC COMPONENT IN TUBERCULOUS MENINGITIS IN THE CHILD. A. PACI, Arch. ital. pediat. e puericolt. **16**:427, 1954.

The complete treatment and cure of tuberculosis meningoencephalitis in children are of interest not only from the neurologic but from even the psychic standpoint. The disorders of the intelligence and character that may follow the disease can last, sometimes lessened, for many years. The greatness of the damage has been shown to be proportional to the neurologic lesions and to the education of the patient. A good well-chosen education seems sufficient to improve the disorders of character.

The author arrives at these conclusions after research and observation on his patients in the Pediatric Clinic of Pisa since 1948. The research and follow-up of the patients have been conducted from the first days of improvement of the disease to many years after.

FROM THE AUTHOR'S SUMMARY.

THE EFFECT OF ISONIAZID ON THE ESTABLISHMENT OF IMMUNITY IN GUINEA PIGS INFECTED BY THE TUBERCLE BACILLUS. A. DEGLI ESPOSTI, Clin. pediat. **36**:202 (March) 1954.

Guinea pigs were infected with tubercle bacilli and treated with isoniazid. The animals, which were reinfected one day after the treatment with the drug had been completed, developed marked areas of tuberculous involvement. On the other hand, animals which were reinfected 12 days after the treatment with the drug was completed showed little tuberculous involvement, indicating that some immunity had been established.

HIGGINS, Boston.

THOUGHTS AND STATISTICS REGARDING ANTITUBERCULOUS VACCINATION. L. MANTEUCCI, Clin. pediat. **36**:211 (March) 1954.

B. C. G. vaccination is not to be preferred to Petragnini's anatuberculin vaccine for the following reasons: 1. B. C. G. organisms are not of the human, but are of the bovine type. 2. B. C. G. organisms do not form or contain the toxins characteristic of the human type organisms. 3. B. C. G. organisms injected into the human body soon die; this is indicated by the fact that the organisms can not be recovered in viable form from the site of the initial injection after the first few days following the injection. 4. The same prophylactic benefit follows the use of dead B. C. G. organisms as when the living organisms were injected. 5. Even although B. C. G. will result in positive tuberculin reactions, it must be admitted that this finding does not necessarily mean that as high an immunity has been obtained as one would have gotten from the injection of killed human type tubercle bacilli.

As compared with unvaccinated children with tuberculosis, children who had been vaccinated by Petragnini's anatuberculin and later developed tuberculosis were found to have a much lower incidence of the severer types, such as miliary, meningeal, and pleuritic.

HIGGINS, Boston.

CONVULSIONS IN CHILDREN WITH TUBERCULOUS MENINGITIS UNDER TREATMENT IN THE PEDIATRIC CLINIC IN BOLOGNA, 1947 TO 1953. A. DEGLI ESPOSTI and G. SILANOS, Clin. pediat. **36**:773 (Oct.) 1954.

Of 268 children treated at the Pediatric Clinic in Bologna, 83, or 31%, had convulsions; 51 had convulsions during the first month of the disease, before any antibiotic therapy had been started. Convulsions were most frequent in the 2- to 5-year-old group (37%) and next in the patients under 2 years of age (34%); they occurred in 26% of the children in the 5- to 7-year-old group, in 19% of those in the 7- to 13-year-old group, and in 6% of the adolescents and adults. Convulsions in children under 5 years usually occurred in the first month of the disease and in older children during the second month or later. Convulsions in the first month were usually due to increased intracranial pressure, to cerebral edema, or to hyperpyrexia; convulsions later may be due to fluid block or to vascular or cortical disturbances. The prognosis in the patients with convulsions was unfavorable; 69% of these patients died. Since the advent of isoniazid therapy, the percentage has dropped to 57%.

HIGGINS, Boston.

THE EARLY RESULTS FROM THE USE OF LARGE DOSES OF ISONIAZID IN THE TREATMENT OF CHILDREN WITH PULMONARY TUBERCULOSIS. T. PERI and E. CLEMENTI, Minerva pediat. **6**:345 (May 15) 1954.

Twenty milligrams of isoniazid per kilogram of body weight in four divided doses was given daily for three months to 25 children with early primary pulmonary tuberculosis. The medicine was well tolerated, and the therapeutic results were very encouraging.

HIGGINS, Boston.

TUBERCULOUS PROCESSES FROM INJECTIONS. M. SAGGESE, Pediatria **62**:103 (Jan.) 1954.

Three cases are reported where tuberculous abscesses appeared at or near the site where penicillin had previously been injected. Two of the children had previously had negative tuberculin reactions and one a positive reaction.

HIGGINS, Boston.

HEPATIC FUNCTION IN TUBERCULOUS MENINGITIS. ROANO ROSSI and LUIGI BARILLI, Riv. clin. pediat. **53**:263 (March) 1954.

Influence of tuberculous disease and antibiotic and chemotherapeutic treatment on various liver function tests is discussed; then effectiveness of experiments carried out is described.

After considering etiology and pathogenesis of the disease, the authors report a statistical study of icterus and hepatic engorgement encountered in patients attending the clinic between 1946 and 1952 and suffering from tuberculous meningitis.

On the basis of their research, the authors came to the conclusion that a clear relationship between hepatic and tuberculous disease exists, even if it is likely to be certain that hepatic insufficiency, more or less evident clinically, has been found in many patients during a certain period.

Therefore the mentioned treatment may not be considered dangerous for the liver function.

FROM THE AUTHORS' SUMMARY.

INTRACUTANEOUS AND PERCUTANEOUS BCG VACCINATION. PREBEN EILERSEN, Acta pædiat. **43**:1 (Jan.) 1954.

Of 357 vaccinated children, 167 were vaccinated by percutaneous scarifications and 190 by intracutaneous injection. One hundred thirty-four have been followed systematically from week to week by Moro patch test and 68 by Mantoux test. The individuals intracutaneously and percutaneously vaccinated showed positive at approximately the same time. The local changes at the site of vaccination have been followed. No major changes were observed in individual scarification vaccination, except for redness, infiltration, and perhaps a little secretion. Intradermal vaccination was very often followed by suppuration and, in isolated cases, abscesses. One hundred sixty-five were postexamined by Moro and Mantoux tests. No certain difference in the allergy obtained was demonstrable. The scars have been inspected. In individual cases with scarification vaccination none or only insignificant scars were found. In individuals subjected to intradermal vaccination, visible scars were often found, in more cases, even thickened, disfiguring scars.

FROM THE AUTHOR'S SUMMARY.

BRONCHOPULMONARY MONILIASIS. AASE SKOGRAND, Nord. med. **51**:276 (Feb. 18) 1954.

This is a report of a one-year-old boy who developed signs and symptoms of bronchopneumonia which was resistant to antibiotics. At autopsy bronchopneumonic foci were found in both lungs. Microscopy revealed numerous Gram-positive spores of Candida albicans, scattered through the sections. Examinations of the pulmonary tissue revealed C. albicans in pure culture. The diagnostic difficulties between bacterial bronchopneumonia and bronchopulmonary moniliasis and the role of the fungus in the reported cases are discussed.

WALLGREN, Stockholm.

CONGENITAL TUBERCULOSIS. JÖRGEN KRINGELBACH, Ugesk. læger **116**:1498 (Oct. 21) 1954.

The author reports a case of congenital tuberculosis successfully treated with chemotherapy. The mother, aged 23, suffered from miliary tuberculosis. The placenta, that was markedly fixed to the uterine wall, was not histologically examined. The baby girl, born 5 weeks too early, with a birth weight of 2250 gm., was first seen on the 16th day of life. She was at that time healthy and displayed no morbid signs, but at 23 days of life she was found to be markedly pale and had irregular respiration. The temperature was slightly increased. Gradually progressive attacks of cyanosis supervened and necessitated oxygen therapy. Ten days after admission a spinal tap showed 77 mononuclear cells. Roentgen examination of the lungs lead to suspicion of infiltration in the right lung and miliary tuberculosis. Treatment with streptomycin, PAS, and isoniazid was started. The tuberculin test was positive. One month after admission, during chemotherapy, otitis occurred, and the purulent secretion contained numerous tubercle bacilli of human type. At 4 months of age she was moved to the same hospital in which the mother was treated for her miliary tuberculosis. The child had had contact with her mother only once after birth. She was discharged healthy. She was cared for in an incubator, and it seems improbable that the mother could have infected her at that time.

WALLGREN, Stockholm.

Diseases of Blood, Heart and Blood Vessels, and Spleen

PROGNOSIS IN IDIOPATHIC THROMBOCYTOPENIC PURPURA OF CHILDHOOD. G. M. KOMROWER and G. H. WATSON, Arch. Dis. Childhood **29**:502 (Dec.) 1954.

This is a study of the prognosis of 43 cases under 15 years of age in Manchester Children's Hospital together with 278 cases reported in the literature dealing with prognosis.

The mortality from acute idiopathic thrombocytopenic purpura is appreciable; in the severer cases (extensive bruising and bleeding other than mild epistaxis) immediate treatment is indicated. Cases of acute onset which survive the first month nearly all recover spontaneously within six months, the majority within three months.

The mortality from chronic idiopathic thrombocytopenic purpura is very small; in such cases splenectomy should be considered only with regard to the degree of disability produced by the symptoms and not because of a very slight chance of the sudden occurrence of grave hemorrhage.

The best guide to the length of course which a case of idiopathic thrombocytopenic purpura is likely to run is the mode of appearance of symptoms and the presence or absence of a history of antecedent infection.

KELLY, Milwaukee.

THE TREATMENT OF HYPOPLASTIC ANAEMIA AFTER CHLORAMPHENICOL. R. MCLAREN TODD, Arch. Dis. Childhood **29**:575 (Dec.) 1954.

The clinical findings in a boy 6 years of age suffering from hypoplastic anemia after chloramphenicol therapy are reported. The details of treatment are described, and it is thought that nicotinamide may have had a beneficial effect on the anemia.

KELLY, Milwaukee.

ACUTE HEMOLYTIC ANEMIA AFTER TREATMENT OF AN ECZEMATOID INFANT WITH RESORCIN. C. GASSER, Helvet. paediat. acta **9**:285 (Oct.) 1954.

The author reports a very severe case of resorcin poisoning with acute hemolytic Heinz-body anemia and methemoglobinemia after two days' treatment of an eczematoid baby with 4% resorcin lotion. He gives a description of the clinical picture and the morphological blood changes. The therapeutic measures are discussed, with special emphasis on the exchange transfusion initiated in 1924 by Robertson.

FROM THE AUTHOR'S SUMMARY.

AN UNUSUAL CASE OF CONSTITUTIONAL THROMBOASTHENIA (GLANZMANN). O. OLIVI and P. MUGNANI, Clin. pediat. **36**:783 (Oct.) 1954.

A 9-year-old boy had the findings of purpura, but with a normal platelet count in the blood. A diagnosis of nonthrombopenic thromboasthenia was made. Treatment with ACTH resulted in improvement in the purpura; this probably was due to a lessening of the vascular fragility, as there was no shortening of the bleeding time and no change in the retraction of the blood clot.

HIGGINS, Boston.

SPLENOPORTOGRAPHY IN CHILDREN. G. SANSONE and B. ROSCIOLO, Clin. pediat. **36**:887 (Dec.) 1954.

A new method for outlining the venous circulation of the spleen is described. A contrasting solution, Ioduron, is injected through a needle directly through the abdominal wall into the spleen. To prevent tearing the splenic tissue, the syringe is not directly attached to the needle, but a rubber tube connects the two. The spleen must be of sufficient size to be firmly held. Films taken by this procedure are shown of cases of Banti's disease, Pick's syndrome, acute leukemia, and hemolytic jaundice; excellent outlines of the splenic veins are shown. Although this procedure is of diagnostic importance, it is not completely innocuous; its use should be restricted to cases in which splenectomy is necessary.

HIGGINS, Boston.

THE COPPER CONTENT OF THE BLOOD IN THE POSTNATAL PERIOD. F. CANTARUTTI and F. PANIZON, Lattante **25**:721 (Nov.) 1954.

The mean copper content of the blood plasma of 13 newborn infants was 79γ per 100 cc. The amount was found to increase gradually until at the age of 2 months the amount was approximately 120γ per 100 cc., at which figure it remained stabilized.

HIGGINS, Boston.

THE DISEASE OF JAKSCH-HAYEM-LUZET: ETIOPATHOGENIC FACTORS AND RECENT THERAPEUTIC MEASURES. F. GRANDI and A. VIANELLO, Lattante **26**:297 (May) 1955.

Two cases of Jaksch-Hayem-Luzet hemolytic anemia are reported in infants, each 2 months of age. The findings were an anemia, mild leucocytosis, enlarged spleen and liver, increasing debility, and the appearance of immature cells in the circulating blood. Iron, liver extract, and vitamin B_{12} were given without there being any clinical improvement. The giving of a folic-acid-like fermentation product, Teropterin, in doses of 2.5 to 5 mg. daily, restored the blood picture and general health of the infants to normal.

HIGGINS, Boston.

ACUTE CIRCULATORY DISTURBANCE WITH ACROGANGRENE IN CHILDREN. LENNART ANDERSSON, Nord. med. **5**:1764 (Dec. 16) 1954.

In a boy aged 5½ years, paleness of the skin and pain in the fingers and toes developed acutely following exposure to moderate cold. This symptom persisted for over one month. Small areas of cutaneous necrosis occurred on the tip of the fingers. Reflex vasodilatation caused only a slight

increase in the skin temperature of the fingers. Despite the sympathicolytic effect of hexamethonium, pain developed in the fingers when they were exposed to cold. The boy was treated with hexamethonium for nine and one-half weeks. He recovered from the acute impairment of circulation, but he still suffers from dead fingers. There is no question of any frostbite. Probably the moderate exposure to cold released a latent Raynaud's disease and the vascular reaction became severe enough to cause thrombosis of the small arteries which became recanalized later.

WALLGREN, Stockholm.

THE SYNDROME OF OCCLUSION OF THE SUPERIOR VENA CAVA. A. HARRESTRUP ANDERSÉN, A. TYBJAERG HANSEN, E. HUSFELDT, ASGER PEDERSEN, and GREGERS THOMSEN, Ugesk. læger **116**:785 (May 27) 1954.

The authors report three cases, one of which was a 9-year-old girl. She was the 8th of 11 children. There was no familial disposition. Since 2 years of age she displayed swelling of the neck and enlargement of the head. The girl easily became dyspneic on exercise. At 6 years of age she was examined at the University Children's clinic of Kiel. She had large distended veins on the front of the trunk. Venogram showed a stenosis of the superior vena cava. Three years later she was admitted to the University clinic of Copenhagen, where it was found that her face was congested and her head enlarged, but not of hydrocephalic type. The circumference of the skull was 64 cm. The shoulders and the overarms were markedly developed in comparison with the lower part of the body. The distended veins on the trunk converged to the umbilicus. She was 125 cm. tall, and her weight was 30 kg. Blood pressure was 120/80; hemoglobin 120 gm. per 100 cc. Roentgen examination of the thorax showed a normal heart shadow and no evident changes in the mediastinum. At the heart catheterization it was found that the pressure in the superior vena cava and vena azygos was 340 mm. of Hg. Repeated angiocardiographies showed that there was an occlusion in superior vena cava between the vena azygos and the right atrium. Anastomosis between the vena azygos and the auricle was performed. The child was discharged healthy. After operation it was easy to put the catheter from the right atrium through the right ventricle to the pulmonary artery. The veins on the upper part of the trunk were still visible but not distended. She was reexamined two years after operation, at which time a marked normalization of the body of the patient had occurred. The hypertrophy of the head, neck, and thorax had almost entirely disappeared.

WALLGREN, Stockholm.

Diseases of Gastrointestinal Tract, Liver, and Peritoneum

PULMONARY FUNCTION IN CYSTIC FIBROSIS OF THE PANCREAS. JOHN R. WEST, SHELDON M. LEVIN, and PAUL A. DI SANT'AGNESE, Pediatrics **13**:155 (Feb.) 1954.

Studies of pulmonary function in patients with chronic pulmonary disease associated with cystic fibrosis of the pancreas have revealed a pattern of dysfunction which may be said to be characteristic of this disease, but which is subject to great variation in severity.

Both ventilatory insufficiency (leading to dyspnea) and disturbances in gas exchange (leading to arterial hypoxia and carbon dioxide retention) may occur. The former would seem to be largely the result of factors which bring about a diminished ventilatory capacity, among which an increased resistance to air flow within the tracheobronchial tree, due to obstruction of the larger and smaller bronchi by accumulated secretions and purulent exudate, is probably most important. Defective gas exchange seems to stem largely from disturbances in the normal relationships of alveolar ventilation to perfusion. This seems in large part due to uneven distribution of tidal air to the alveoli as a result of bronchial obstruction, although concomitant variation in the distribution of blood probably occurs also.

In general, the severity of the impairment of pulmonary function closely parallels the chronicity and severity of the characteristic secondary bronchial and pulmonary infections. The treatment of these constitutes, logically, the major effort in therapy.

FROM THE AUTHORS' SUMMARY.

TRICHOBEZOAR. F. C. FRIEDLANDER and P. KUSHLICK, Arch. Dis. Childhood **29**:556 (Dec.) 1954.

A case of trichobezoar in a 9-year-old white girl is reported.

A classification of bezoars is given, and the clinical and radiological features and laboratory findings are discussed.

KELLY, Milwaukee.

CHOLECYSTOGRAPHY WITH "BILIGRAFIN" IN INFANTS. P. TOLENTINO and A. DE MAESTRI, Lattante **25**:129 (March) 1954.

Biligrafin is a cholecystographic medium adapted for intravenous use; it contains 64.3% iodine and is chemically quite similar in structure to Telepaque, which is for oral use. Injections of Biligrafin were given to 10 infants. Doses of 1.5 to 2 cc. per kilogram appeared to give the best results radiographically. The gall bladder was demonstrable clearly in eight of the cases; the other two infants were developing an infectious hepatitis, and no shadow of the gall bladder was outlined. In children, the main use of this procedure is for testing liver function.

HIGGINS, Boston.

FUNCTIONAL STENOSIS OF THE DUODENUM IN THE NEWBORN INFANT. M. BOLLETTI, Lattante **25**:163 (March) 1954.

Three cases of functional stenosis of the duodenum in newborn infants are reported. After the initial passage of meconium, no stools were passed, and practically all food and fluids were vomited projectively. X-ray films revealed that the stenosis was in either the second or third portion of the duodenum. Each child recovered without the necessity of surgical intervention. The stoppage was apparently spastic in nature.

HIGGINS, Boston.

TWO CASES OF ATRESIA OF THE BILE DUCTS. G. ACETO, Lattante **25**:173 (March) 1954.

Two infants, 2 and 3 months of age, were operated upon for congenital stricture of the bile ducts. In one case, the stricture was in the hepatic duct a short distance above the cystic duct; the dilated duct was implanted into the second portion of the duodenum with the aid of a politene tube. This infant appeared perfectly normal two months later. In the other case, the strictures were more extensive in the hepatic ducts; a dilated hepatic duct was implanted into the stomach; the infant seemed to do very well for a few days, but on the 20th postoperative day died of bronchopneumonia.

HIGGINS, Boston.

THE TREATMENT OF MINOR HEPATIC DYSFUNCTION IN CHILDREN. P. POSTERARO, Minerva pediat. **6**:32 (Jan. 15) 1954.

Signs of minor hepatic dysfunction in children may often follow infection where sulfonamides or antibiotics have been given. The symptoms may include pallor, subicteric sclerae, slightly enlarged liver, asthenia, anorexia, fat indigestion, and urticaria. The author has treated 50 children with this condition with very favorable results by a preparation containing betaine, choline, and vitamins B_1 and B_{12}.

HIGGINS, Boston.

THE TREATMENT OF ACUTE INTESTINAL DISTURBANCES IN INFANTS BY THE LOCAL ACTION OF A SULFONAMIDE PREPARATION. S. CAVALIERI and F. SACCOMANI, Minerva pediat. **7**:236 (Feb.) 1955.

Thirty-nine infants with gastroenteritis were treated by a mixed preparation of sulfonamide drugs — formosulfamerazine, formosulfathiazol, phthalylsulfathiazol, and sulfaguanidine; the clinical results were satisfactory. The fever had usually receded before the stools had become of normal consistency. Any initial loss of weight was soon recovered. There was a tendency for the intestinal flora to show an increased percentage of Gram-positive organisms. The belief is expressed that the therapeutic action of the drugs was largely in the intestinal tract, since the sulfonamidemia was considerably less than the minimum bacteriostatic level.

HIGGINS, Boston.

A CLINICAL AND STATISTICAL REVIEW OF FIFTY-TWO CASES OF CATARRHAL JAUNDICE IN CHILDREN. E. SEGAGNI and P. N. SARIO, Minerva pediat. **7**:508 (April 21) 1955.

Fifty-two children with catarrhal jaundice were hospitalized in the Pediatric Clinic in Turin over a period of nine years. About one-half of these cases occurred in the years 1951 and 1952; an increased incidence was reported also for adults in these same years. There was found no seasonal prevalence of the disease. Nine of the cases occurred in infants under 1 year of age,

and all but six in children under 7 years. Eighty-eight per cent of the cases lasted 10 days or less. Fifty-two per cent were afebrile. The illnesses were severest in the eight infants under 8 months of age; they had high fever (39 to 40 C); one died. Treatment with antibiotics was resorted to only in the severer cases, making an evaluation of their efficacy difficult. HIGGINS, Boston.

PSEUDO-OCCLUSION IN THE NEWBORN: REVERSIBLE CONGENITAL ILEUS. E. ROVIRALTA. Acta pediát. españ. **13**:217-244 (April) 1955.

The author discusses the various anatomopathological conditions which may cause intestinal occlusion in the newborn infant, with ample roentgenograms, but he also claims there is a syndrome in the premature and the newborn infants in general which is a pseudo-occlusion and is reversible. He presents a series of cases in which this was true. While it is very necessary to have surgical intervention if there is some malformation incompatible with life, careful study should be made on those where this is not necessary and treatment instituted. He also gives some cases in which surgery was necessary. ALLEN, Santa Fe, N. Mex.

Nervous Diseases

METHYLPHENYLSUCCINIMIDE (MILONTIN) IN EPILEPSY. DOUGLAS T. DAVIDSON JR., DESARE LOMBROSE, and CHARLES H. MARKHAM, New England J. Med. **253**:173 (Aug. 4) 1955.

Methylphenylsuccinimide (Milontin) was given to a selected group of 296 patients in a period of three years. No serious side-effects were encountered. Sedation, ataxia, irritability, and rash, in that order, occurred in 10% to 5%.

Among 249 patients adequately followed, seizure control was most effective for persons with pure petit mal and for those with three-per-second spike-wave discharges in the electroencephalogram. Petit mal attacks were reduced by more than half in 40% of patients, in 36% if a "dione" had been employed in the previous control period, and in 58% if it had not been used.

Convulsions were also fewer (27% of grand-mal patients had less than half as many). However, in these cases, anticonvulsant drugs were also employed.

Because blood dyscrasia, liver toxicity, psychosis, or other serious side-effects have not been encountered, this drug may logically be used as the initial treatment of pure petit mal.

FROM THE AUTHORS' SUMMARY.

ACUTE DISSEMINATED ENCEPHALOMYELITIS TREATED WITH ACTH. BEN SELLING and EDWARD MEILMAN, New England J. Med. **253**:275 (Aug. 18) 1955.

Acute disseminated encephalomyelitis is a recognized disease of both children and adults. The symptoms and signs that characterize it are due to widespread damage to the white matter of the central nervous system. It may follow exanthemata and vaccinations but may occur without recognizable antecedent.

The authors treated a young adult with this disease, utilizing a total of 2785 mg. of ACTH over a 40-day period. Prompt relief of symptoms both after initial treatment and after a relapse suggest that ACTH and adrenal steroids are of value in the treatment of this dangerous disease. A hypersensitivity reaction is suggested as the cause of acute disseminated encephalomyelitis.

Fifteen patients who suffered a total of 17 episodes of encephalomyelitis have been treated with ACTH or cortisone, with beneficial results in 10 patients and 12 episodes.

This accumulated experience, collected from the literature, is briefly described.

WHEELOCK, Washington, D. C.

CONGENITAL ENCEPHALOPATHIES. A. BALLABRIGA, Arch. pediat., Barcelona **5**:285-335 (Nov.-Dec.) 1954.

This is one of a series of detailed description of encephalopathies which may be due to some deleterious conditions during gestation, during the process of birth, or immediately thereafter. Several definitions by different investigators are given. The name cerebral palsy has been given to this group, but the author discusses not only the upper motor neuron lesions but other conditions which may be present, such as mental retardation, convulsions, sensory lesions, and defects resulting from these which lead to behavioral and language difficulties.

He gives the classification according to Phelps-Fay and the one devised by Perlstein, also the Perlstein-Bennet study of the specific etiological factor to the malformation.

He discusses the diagnosis, differential diagnosis, and areas of the brain affected in each type, with photographs of children in each category.

He also includes the hereditary degenerative diseases and points out the need for a very careful family history as well as the child's history. He gives lists of pertinent questions which should be asked in regard to conditions as in prenatal life and delivery of the baby, as well as investigation of appearance as a newborn baby.

The developmental steps should be carefully tabulated, for in a child with any of these defects development will not follow the expected pattern. He outlines five signs to watch for in development of motor activities.

He discusses the value of electroencephalograms in young children and means of diagnosis of hearing defects. The dependence of language development on (1) mental capacity, (2) condition of hearing, and (3) normal functioning of the organs of speech is discussed, with comments about conservation of hearing and other therapeutic measures.

The testing of the child's intelligence cannot be done by ordinary measures, and the author discusses some of the means of evaluation of intelligence from such tests as the Pitner-Patterson scale. No test should be considered final, as some of these children develop far beyond early expectations.

Last, he outlines the type of encephalopathy which leads to precocious puberty.

ALLEN, Santa Fe, N. Mex.

A CURED CASE OF MENINGITIS DUE TO LISTERIOSIS. H. FLAMM, P. KREPTER, and H. HARAZIM, Wien. klin. Wchnschr. **66**:553 (Aug. 13) 1954.

A purulent meningitis in an 8-year-old boy is described. In the sediment of the cerebrospinal fluid were Gram-positive cocci-like elements, and from the fluid, micro-organisms could be cultured which proved to be Listeria monocytogenes of the serological Type 1. The characteristics of this micro-organism are given, and the various clinical pictures of listeriosis in man are discussed. The patient cited responded readily to a combined treatment with penicillin and a sulfonamide.

AMBERG, Rochester, Minn.

THE SO-CALLED "ABSENCE": DIAGNOSTIC AND THERAPEUTIC CHIEF PROBLEM OF EPILEPSY. ERNST NIEDERMEYER, Wien. klin. Wchnschr. **66**:845 (Nov. 5) 1954.

This paper gives in a table the most important differentiation of petit mal from involvement of the temporal lobe (psychomotor epilepsy), clinical as well as by electroencephalography. Drugs for treatment are selected on this basis.

AMBERG, Rochester, Minn.

CHILDREN OF MOTHERS TREATED BY ELECTROSHOCK DURING PREGNANCY. HANS FORSMAN, Nord. med. **52**:1515 (Oct. 28) 1954.

A follow-up of 16 children whose mothers were given electric convulsive therapy during gestation is presented. All the children, (the eldest 6 years, 9 months, the youngest 16 months) were mentally normally developed and in good general state of health.

WALLGREN, Stockholm.

AGENESIS OF THE CORPUS CALOSUM. KAREN ELSE FOGHT-NIELSEN, GREGERS THOMSEN, and JØRGEN WESTERDAHL, Ugeskr. læger **116**:1317 (Sept. 16) 1954.

The authors report 4 cases of agenesia of the corpus calosum in children 2½-16 years of age. In a girl 11½, there was no clinical sign of cerebral lesions, and the girl was well developed mentally. In the other three cases the mental and psychomotoric development had been markedly retarded. The encephalographic findings were typical for agenesia of the corpus calosum.

WALLGREN, Stockholm.

FEVER CONVULSIONS IN CHILDREN: INCIDENCE AND PROGNOSIS. C. FRIEDERICHSEN and J. MELCHIOR, Ugeskr. læger **116**:1419 (Oct. 7) 1954.

The authors report 405 children with fever convulsions. Of these, 82% had displayed their first attack within the first three years of life, the majority at about 18 months of age. Fifty-five per cent of these children were boys. In 62% of the cases the fever was due to acute upper

respiratory infections. Twelve per cent of the children were readmitted with fever convulsions. Out of all admitted children under 7 years of age, in a five-year period, 30% were febrile, and of these, every ninth child (in all 405) suffered from convulsions. Seventy-seven per cent of these children were studied in a follow-up. Sixty-eight per cent of them had been healthy since their discharge from the hospital. In 2.8% epilepsy had developed. WALLGREN, Stockholm.

ELECTROENCEPHALOGRAPHIC FINDINGS IN CHILDREN WITH FEBRILE CONVULSIONS. RAGNHILD BJERGLUND and SVEN BRANDT, Ugeskr. læger **116**:1423 (Oct. 7) 1954.

Of 129 children who had had one or more epileptic seizures exclusively in connection with fever, 25% displayed abnormal EEG pattern. The abnormalities were most frequent in girls and in the age group 3-4 years. The incidence was highest in the group with more than one attack and slightly higher following prolonged convulsions than after fits of short duration. The incidence was not higher in children examined shortly after an attack than in children examined after the lapse of a long interval. The abnormalities may disappear with time, may persist unchanged, or become accentuated. A few children in whom EEG changes were initially normal showed abnormalities after subsequent seizures. The authors maintained that the EEG findings indicate that febrile convulsions actually are epileptic seizures, although in the majority of cases caused by a mild form of epilepsy, with fairly good prognosis. WALLGREN, Stockholm.

Diseases of Genitourinary Tract

THE INFLUENCE OF EVENTS DURING THE LAST FEW DAYS IN UTERO ON TISSUE DESTRUCTION AND RENAL FUNCTION IN THE FIRST TWO DAYS OF INDEPENDENT LIFE. R. A. MCCANCE and E. M. WIDDOWSON, Arch. Dis. Childhood **29**:495 (Dec.) 1954.

Following a prolonged and difficult labor, full-term and postmature infants have been found to show some or all of the following abnormalities: (*a*) an increased destruction of body protein during the first 48 hours of life; (*b*) a reduced glomerular filtration rate, a poor urea clearance and a low urine volume; (*c*) a high ratio of nitrogen potassium in the urine; (*d*) a large excretion of inorganic phosphate during and immediately after birth.

All the characteristic features may not be found in each case, and the complete "syndrome" may be due to multiple causes. KELLY, Milwaukee.

NEONATAL ASCITES ASSOCIATED WITH URETHRAL OBSTRUCTION. N. E. FANCE and E. H. BACK, Arch. Dis. Childhood **29**:565 (Dec.) 1954.

Two baby boys with congenital urethral valves and ascites occurring in the neonatal period are reported. In one case muscle in the wall of the bladder was partially lacking, in the other the bladder ruptured.

It is suggested that in the presence of urethral obstruction, ascites is due to the accumulation of urine in the peritoneal cavity following leakage or transudation from the urinary tract.

KELLY, Milwaukee.

EPIDEMIC NEPHROPATHIA. BJARNE TUNGLAND, Nord. med. **51**:635 (May 6) 1954.

The author reports 28 cases of epidemic nephropathia (26 males and 2 females), observed at a local hospital in Norway between 1948 and 1954. The majority of cases occurred in the wintertime 1948-1949. Headache and backache were the commonest symptoms; in 16 patients abdominal pain predominated. Blood pressure was normal; there was no edema. Proteinuria was present in all cases but one. Hematuria was absent. Twenty-three cases had azotemia. The sedimentation rate was increased in 21 patients. On an average the proteinuria subsided 11 days and the azotemia 18 days after onset. The commonest diagnoses were acute nephritis and acute abdomen. The incubation period lasted from two to six weeks. The prognosis was good.

WALLGREN, Stockholm.

AMINO ACIDS AND AMINO-ACIDURIA. ARNLJOT DRABLØS, Nord. med. **51**:699 (May 20) 1954.

This is a report of a 15-month-old girl with typical signs of cystinosis and two other infants 2 years and 11 months old, respectively, with amino-aciduria; the latter was thought to be due to a nephropathia with functional deficiency of the tubulae to reabsorb amino acids, phosphate, and alkali. The case of cystinosis was the first one published from Norway.

WALLGREN, Stockholm.

THE INCIDENCE OF SURGICAL CONDITIONS OF THE URINARY TRACT IN CHILDREN WITH PYURIA. JÖRGEN KRINGELBACH, Ugeskr. læger **116**:1533 (Oct. 28) 1954.

The author reports on 72 children suffering from pyuria, of which 37 had recurrent pyuria. Scarcely one-third of them were boys. In 16 children changes in the urinary tract were found as a probable cause of the recurrence of the pyuria. Operative intervention was undertaken in seven of the children, and it was recommended in two other cases. WALLGREN, Stockholm.

TREATMENT OF CHRYPOTORCHISM. MOGENS ANDREASEN, HENNING ANDERSEN, and C. HANSTED, Ugeskr. læger **116**:1689 (Dec. 2) 1954.

The authors report 38 cases. Undescended testes complicated by hernia as well as superficial inguinal ectopia of the testes should be operated upon when the diagnosis is established. Unilateral undescended testis should be operated when the first signs of puberty become evident. Bilaterally retained testes are treated with hormones at the beginning of puberty; should no descent occur within two months after this therapy, operation is undertaken.

WALLGREN, Stockholm.

Diseases of Ductless Glands; Endocrinology

IDIOPATHIC HYPERCALCAEMIA IN AN INFANT. I. M. P. DAWSON, W. S. CRAIG, and F. J. C. PERERA, Arch. Dis. Childhood **29**:475 (Dec.) 1954.

A case of idiopathic hypercalcemia of a severe and prolonged type in a boy was studied clinically and at necropsy.

Clinical and biochemical findings included failure to thrive, lassitude, generalized hypotonia, irregular pyrexia, hypertension with a pronounced cardiac murmur, craniofacial asymmetry, and excessive irregular deposition of bone. Serum calcium, blood cholesterol, and blood urea levels were raised, and there was evidence of renal impairment.

Histological findings in the kidneys included deposition of calcium in and around distal and collecting tubules, vacuolation of proximal tubule cells, and hyaline glomerular changes. Abnormal histological changes in the bones were not seen. There was no evidence of metastatic calcification. An unexplained feature was calcium deposits in the pulp of certain incisor teeth. The parathyroid glands were normal.

Renal changes are regarded as secondary to hypercalcemia, which it is suggested may have resulted from excessive absorption of calcium by the alimentary tract.

KELLY, Milwaukee.

THE VALUE OF RADIOIODINE (I^{131}) IN JUVENILE MYXOEDEMA DUE TO ECTOPIC THYROID TISSUE. E. M. MCGIRR and JAMES H. HUTCHISON, Arch. Dis. Childhood **29**:561 (Dec.) 1954.

The clinical features of hypothyroidism in two children who were investigated with I^{131} are presented.

The I^{131} studies indicated the absence of thyroid tissue in the normal site and revealed that the only thyroid tissue was situated above the hyoid bone at the base of the tongue.

The value of scanning the neck for I^{131} accumulation in patients with midline neck swellings and in unexplained cases of juvenile myxedema is discussed.

A probable explanation of the presence of appreciable amounts of protein-bound I^{131} in hypothyroid patients with scanty thyroid tissue is considered. KELLY, Milwaukee.

HYPOGONADISM IN BOYS. A. PRADER, Schweiz. med. Wchnschr. **85**:737-745 (July 30) 1955.

The various forms of hypogonadism in boys are discussed with regard to diagnosis and treatment. Perusal of the paper will be worth while. AMBERG, Rochester, Minn.

THE EFFECT OF CORTISONE ON THE GROWTH, INTERMEDIARY AND NITROGEN METABOLISM, AND ELECTROLYTES IN CASES OF DYSTROPHIC INFANTS. O. OLIVI and M. P. PRODI, Clin. pediat. **36**:919 (Dec.) 1954.

Seven dystrophic infants were given 5 or 10 mg. of cortisone intramuscularly daily over a period of 10 days. Each infant showed a marked gain in weight almost immediately on discontinuing the medicine. Chemical studies revealed that these gains were referable to the fat, carbohydrate, and protein metabolism and not to the electrolytes or water balance. The cortisone may be said to overcome a resistance to weight gain. HIGGINS, Boston.

THE EFFECT OF ACTH ON THE BLOOD CALCIUM AND POTASSIUM. E. SEGAGNI, Minerva pediat. **7**:295 (March 10) 1955.

Twelve children, whose ages varied between 2½ and 11 years, were given about 1 mg. per kilogram of body weight of ACTH over a period of 4 to 10 days. There were no marked nor consistent changes in the calcium or potassium content of the blood serum as a result of this medication.

HIGGINS, Boston.

A CASE OF CONGENITAL GOITER. B. E. DI GIACOMO and M. R. STALLONE, Minerva pediat. **7**:556 (April 28) 1955.

There was no family history of goiter, except for the mother and her four children. The mother had a simple nontoxic goiter, which became larger and caused some pressure symptoms while she was carrying each of her four children. Each of the four children had a goiter at birth; in the case of the two older children, it had receded after about one month; the goiter of the third child also became smaller, but was still apparent at the age of 4 years. The case of the fourth child is discussed at length, having been followed from the age of 1 day to 7 months; the goiter was still present, but very much smaller. In all of the children, the goiters were asymptomatic. The family did not live in an area where goiter was endemic. It seems probable that the goiters in these children were due to a familial hereditary predisposition.

HIGGINS, Boston.

CHILDREN OF DIABETIC MOTHERS. ARNE KOSS, Tidskr. norske lægefor. **74**:453 (July) 1954.

A case is reported in which electrocardiographic evidence of hypopotassemia was demonstrated following the occurrence of sudden collapse 14½ hours after birth. Potassium therapy was instituted, and the electrocardiographic pattern was normalized within three hours after the first administration. The treatment was continued for five days. The further course was uneventful.

WALLGREN, Stockholm.

Cutaneous Diseases; Allergy

THE PROPHYLAXIS OF ALLERGIC DISEASE WITH SPECIAL REFERENCE TO THE NEWBORN INFANT. JEROME GLASER, New York J. Med. **55**:2599 (Sept. 15) 1955.

Glaser says that most allergic diseases begin in childhood and ascribes this to the diet of the pregnant woman. He asks his pregnant mothers to avoid eggs and custards, to drink a pint of boiled milk each day, and to eat no cheese. A variety of meats is allowed for protein content, and he adds calcium and phosphorus to their diets as necessary. Lack of breast feeding (and the substitution of cow's milk, therefore) is contributory to skin conditions (eczema) in infants. Egg yolk is not allowed the infant until the sixth or ninth month, during which period some immunity against egg yolk may be expected. The same is true for egg white. Many items ingested by the nursing mother are present in the mother's milk. Therefore, the parenteral diet during pregnancy should be maintained during the first postnatal months. There is no condemnation of cow's milk, for it is a "great gift to mankind," but in certain infants it is unwelcome and may cause various troubles in the digestive tract or skin. However, the gradual abandonment of the female breast as nature's food emporium for infants may possibly be responsible for some evils now overlooked as to etiology.

ABSTRACTOR'S COMMENT: ENT specialists doing allergy must often be puzzled as to management of allergies in very young patients. Since anything which gets into the mother's blood stream may affect the infant for good or ill, what about tobacco and alcohol, so commonly in use these days by women as well as by men?

I. W. VOORHEES, New York [A. M. A. ARCH. OTOLARYNG.].

ASTHMA IN CHILDREN. THEODOR WALTHER, Nord. med. **52**:1571 (Nov. 11) 1954.

There was a four times higher incidence of diabetes mellitus in families presenting various allergic conditions than in families free of allergic diseases. Rheumatic fever was observed without exception among the families in which different allergic manifestations occurred. On

the base of personal observations, the author maintains that of all the allergic diseases both in the families and in the children themselves, atopic dermatitis in infancy and/or in early childhood seems to have a decisive influence upon the frequency and time of onset of asthma and perhaps also upon the special clinical forms. Adenotomy and tonsillectomy should be avoided in most cases of asthma, as the tonsillar hyperplasia and adenoid vegetations are usually the result of the asthmatic condition itself and not the contrary. Serious complications in asthma are very rare. Atelectasis seldom persists longer than two to six months. Bronchiectasis is rare. Status asthmaticus was found in about 1%, and there were no deaths. In status asthmaticus a large single dose of cortisone or ACTH should be given as soon as possible, followed if required by a further one or two smaller doses. Relief usually begins within 24 hours after treatment. More frequent use of these drugs in regular asthma in children should be avoided.

WALLGREN, Stockholm.

INCIDENCE OF ASTHMA IN SCHOOL CHILDREN. EILERT EILERTSEN, Tidskr. norske lægefor. **74**:322 (May) 1954.

Among 6032 children aged 7 years, there was found an incidence of asthma of 1.77%. The study was based upon detailed questionnaires sent to the parents and verified by medical examination. The incidence of asthma in the general population of the same Norwegian city (Bergen) was estimated to about 2%.

WALLGREN, Stockholm.

THE PERSISTENCE OF ACQUIRED HYPERSENSITIVITY. J. P. NIELSEN and KAMMA BANG, Ugeskr. læger **116**:241 (Feb. 18) 1954.

Reexamination after 2-19 years (mean 13.5) with standardized allergen patch tests of a group of eczematous patients revealed ultimate loss of hypersensitivity in about 60%. An investigation into the relationship between the offending agent and alterations in hypersensitivity and the occurrence of eczema showed that elimination of the offending agent resulted in loss of hypersensitivity in most cases although eczematous eruptions continued to appear for a number of years. At the final examination, however, the number of cured cases exceeded the number of cases which continued to have eczema. Continuance of exposure to the offending agent resulted in persistence of hypersensitivity in most cases, but even so there was a decrease in the incidence of eczematous eruptions.

WALLGREN, Stockholm.

Teeth and Dentistry

FLUORIDATION. F. B. EXNER, Northwest Med. **54**:1105 (Oct.) 1955.

Part 2 of a three-part discussion of fluoridation by an outspoken opponent of Fluoridation of Community Water Supplies is well worth reading. The author reviews quite critically articles and statistics of proponents of fluoridation of community water supplies. His analysis and interpretation of statistics presented in favor of this form of medication should be studied by all interested in this problem.

DOCTOR, Seattle.

THE EFFECT OF RICKETS AND SPASMOPHILIA ON THE PERMANENT DENTAL OCCLUSION. PER SELANDER and HANS GRAHNÉN, Nord. med. **51**:197 (Feb. 4) 1954.

The authors report a comparison between three groups of children and young people. One group consisted of 62 individuals who had had verified rickets in early life; one group of 56 individuals who had verified spasmophilia in early life, and one control group of 64 individuals who on examinations in children's hospitals during early life had not exhibited any clinical signs of diseases. Symmetric enamel defects occurred in about 25% of the rachitic group, in about 75% of the spasmophilic group, and about 3% of the control group. The only teeth affected were incisors, canines, and six-year molars. It is hardly conceivable that any factors other than those mentioned are the cause of the enamel defects. There was no difference between the severity of the dental hypoplasia in the rachitic and spasmophilic cases. Increased disposition to caries is not encountered after either rickets or spasmophilia.

WALLGREN, Stockholm.

Miscellaneous

YOUTHFUL SUICIDE ATTEMPTS: PART 2. DOUGLAS POWERS, Northwest Med. **53**:1231 (Dec.) 1954.

This is the second of two articles expressing the belief that thwarted suicide attempts in the young age group are relatively amenable to therapy if approached correctly. The importance of the physician's attitude and the early establishement of a sympathetic atmosphere are stressed as essential to initiating successful therapy.

DOCTOR, Seattle.

ADVANCES IN INHALATIONAL THERAPY. M. S. SEGAL, A. SALOMON, C. WOODS, and J. A. HERSCHFUS, South. M. J. **47**:888 (Sept.) 1954.

The authors discuss the use of inhalational therapy in both adults and children. They specifically discuss continuous aerosol treatment, using water, Alevaire, antibiotics, and alcohol and the use of enzyme aerosols of pancreatic deoxyribonuclease. They also discuss the use of exsufflation utilizing positive-negative pressures for the production of rapid expiratory airflow rates as an aid in the evacuation of retained bronchopulmonary secretions.

LOGAN, Rochester, Minn.

LOCAL COMPLICATIONS IN INTRAVENOUS THERAPY. SUBCOMMITTEE INVESTIGATING INTRAVENOUS INFUSIONS, Great Ormond St. J. (No. 7) pp. 43-55 (June) 1954.

After study of 851 infusions it was found that the incidence of complications is directly proportionate to the duration of the infusion. Red rubber tubing should be avoided, and all dextrose-containing fluids should be neutralized. Thrombophlebitis is the commonest and most important complication.

MCGUIGAN, Evanston, Ill.

A SURVEY OF ACCIDENTAL POISONING IN CHILDREN DURING THE PAST THREE YEARS AT THE TOWNSVILLE GENERAL HOSPITAL. M. ELYAN, M. J. Australia **2**:513-514 (Sept. 25) 1954.

Cases of poisoning seen over a three-year period are reviewed. There were no deaths. Sixty-three per cent were due to kerosene, one to arsenic, and the rest due to varying medicine, brass polish, and unknown agents.

MCGUIGAN, Evanston, Ill.

A CASE OF RETICULOSIS WITH A PROTRACTED DEVELOPMENT OF THE DISEASE. J. L. KEYZER, Acta pædiat. **43**:478 (Sept.) 1954.

The author reports a case of reticulosis of the skin and lungs without fever (Julien Marie) and with complete recovery in a 2-year-old boy.

FROM THE AUTHOR'S SUMMARY.

COMPLICATIONS DURING TREATMENT WITH TRIDIONE IN CHILDREN. BJÖRN REDIN, Nord. med. **49**:563 (April 17) 1953.

The author reports two cases. One, a 7-year-old girl, developed a nephrotic syndrome 10 months after the start of treatment but recovered gradually when medication was stopped. The other case, a girl aged 11, presented an alarming reaction after one month of treatment, including exfoliative dermatitis, signs of hepatic damage, and agranulocytosis ending in death.

WALLGREN Stockholm.

SUBCUTANEOUS RUPTURES OF ABDOMINAL ORGANS IN CHILDREN. LARS ENGSTRÖM, Nord. med. **51**:575 (April 22) 1954.

The author reports 60 cases of subcutaneous abdominal injuries in children. Rupture of the kidney occurred 25 times, of the spleen 16, of the liver 12, of the pancreas 4, of the intestine 4, and of the bladder 3 times. The rupture of the kidney healed without surgical treatment in all cases. In one case renal colic was produced by the passage of a blood clot. Splenectomy was performed in 15 of the 16 cases of rupture of the spleen. In two of these cases with subcapsular hemorrhage severe peritontitis supervened a few days after the accident. The liver was sutured

in 6 of the 12 cases of rupture of the liver. In three cases of traumatic pancreatitis, intermittent pain, rise of temperature, vomiting, and loss of appetite supervened. Laparotomy and drainage were performed, resulting in rapid improvement of the patients' condition. Three of the 60 patients died because of severe complicating injuries to the skull and thorax.

WALLGREN, Stockholm.

EYE ACCIDENTS AMONG CHILDREN IN STOCKHOLM DURING A FIVE-YEAR PERIOD. H. EUGÉN STRÖMBERG, Svenska läk.-tidning. **51**:1883 (July 16) 1954.

The total of eye accidents during this period was 276, of which 223 concerned boys. The incidence was 3.2-3.8 in 10,000 children. In the suburbs of Stockholm the incidence was higher. Most children were between 7-11 years of age. More than 25% of all children admitted to hospital for eye accidents had perforating damage to the eye. Most damaged are produced by arrows and other projectils. In 13% the sight on the damaged eye was decreased to less than half-blindness, and in an additional 5%, the sight had been seriously decreased. Enucleation had to be done in 18 cases.

WALLGREN, Stockholm.

POISONING IN CHILDREN. BERTIL LINDQUIST, Svenska läk.-tidning. **51**:2080 (Aug. 13) 1954.

This is a report of 127 poisonings in children seen at the pediatric clinic of the University of Lund during a 10-year period. In 40 cases severe symptoms of intoxication occurred, especially from drugs. In about 85%, negligence on the part of the parents was the cause of the poisoning, and in about a quarter of the total number of cases it was question of an unlawful mode of conservation of the drug or another type of severer carelessness. The author emphasizes the need of repeated enlightment of the public and that attention should be focused upon the mode of preservation of different poisons, especially medicines.

WALLGREN, Stockholm.

SUBCAPSULAR RUPTURE OF THE LIVER IN CHILDREN. PER OMTVEDT, Tidskr. norske lægefor. **74**:560 (Sept. 1) 1954.

This is a report of three cases of subcapsular rupture of the liver in children aged 4, 6, and 12 years. A few hours after a traumatic lesion against the abdomen the children fell ill with pains in the upper part of the abdomen, vomiting, and progressive anemia. The liver was found to be markedly enlarged. Blood transfusions produced a regression of the signs, and all three children were discharged healthy. The author stresses that subcapsular rupture of the liver occurs only in children because of the more elastic capsule in this age.

WALLGREN, Stockholm.

News and Comment

GENERAL NEWS

Specialists Certified by The American Board of Pediatrics, Inc.—The following physicians were certified as specialists by The American Board of Pediatrics, Inc., in Atlanta, on March 2, 3, and 4, 1956.

Alberts, Marion Edward, Des Moines, Iowa.
Black, Grady E., Griffin, Ga.
Buess, John Edward, New York.
Couchman, Mary Pucci, Mt. Pleasant, Iowa.
Cranny, Robert LeVerne, Oklahoma City.
DeMaria, William J., Durham, N. C.
Diamond, Eugene Francis, Chicago.
Dreher, Richard L., Salina, Kan.
Ellis, Noel Arlis, El Paso, Texas
Evans, Alton Norman, Alexandria, La.
Furst, William Dunton, Odessa, Texas
Goodman, Harold, Chicago.
Greenwold, Warren E., Urbana, Ill.
Hanson, Homer Harvey, Carbondale, Ill.
Heyn, Ruth Mareta, Ann Arbor, Mich.
Holcomb, Thomas Murray, Montgomery, Ala.
Howell, Doris Ahlee, Durham, N. C.
Jackson, Lee, Cleveland.
Jacobson, Warren R., Grand Junction, Colo.
Joseph, Alfred, College Park, Ga.
Kelly, Walter Clyde, Jacksonville, Fla.
Kushner, Joseph Harold, San Francisco.
LaRue, Raymond Abram, Lakeland, Fla.
Lewis, John H., Jr., Cleveland.
Matta, Enrique L., Jr., San Juan, P. R.
McCanless, Edgar Eugene, Barksdale Air Force Base, La.
McFarland, Louis R., Hot Springs, Ark.
Merkin, Albert C., Chicago
Merrill, Robert Erle, Tullahoma, Tenn.
Miller, Richard Braun, Memphis.
Modjeska, Gerald S., Chicago.
Morgenthau, Joan Elizabeth, New York.
Niccum, Warren LeClair, Columbia City, Ind.
Nicholson, Ruth Lynn, Little Rock, Ark.
Ortega, Gimel, Miami, Fla.
Paterson, Lester C., Muskegon, Mich.
Pfundt, Theodore Robert, Oklahoma City.
Rabinowitz, Haskell I., McAllen, Texas.
Reiquam, Charles William, Denver.
Rhyne, Marie Britt, Lumberton, N. C.
Runge, Gretchen Herrmann, Austin, Texas.
Sarazen, Paul Mark, Jr., Shelby, N. C.
Sarracino, John B., New York.
Sawyer, Bina Elizabeth, New York.
Schmidt, Donald G., Denver.
Schwartz, Tillie, Hollis, N. Y.
Seymour, Charles Floyd, Fort Lauderdale, Fla.
Sheridan, Robert John, Rocky Mount, N. C.
Shope, William Benner, Greensburg, Pa.
Statham, George Wilkes, Decatur, Ga.
Stewart, C. Scott, San Antonio, Texas.
Sullivan, Margaret Patricia, Houston, Texas.
Tiller, Ralph E., Columbus, Ga.
Waites, Lucius, Jr., Chicago.
Walter, Ruth Perkins, Santa Monica, Calif.
Warner, Arthur L., Tucson, Ariz.
Warner, Charles Lloyd, Evansville, Ind.
Watkins, Thomas W., Fort Hood, Texas.
Wicksman, Robert S., Chelsea, Mass.
Wilkes, William Albert, Augusta, Ga.
Woods, Helen Haury, Corpus Christi, Texas.
Yockey, William Byran, Pittsburgh.
Zee, Maurice L., Chicago.
Zuleger, Frank Goddard, Glen Cove, N. Y.

Special certificate—foreign:

Choy, Nai-Shum, Cleveland.

ANNOUNCEMENTS

Course in Pediatric Oncology.—The pediatric department of Memorial Center for Cancer and Allied Diseases announces that the annual comprehensive three-day course in pediatric oncology for pediatricians, general practitioners, and health officers will be held April 25, 26, and 27, 1956. The purpose of this course is to review current concepts regarding the neoplastic diseases of children, particularly as to diagnosis, differential diagnosis, and management, and to indicate the importance of the clinician's role in the control of cancer in childhood.

Case demonstrations, clinics, and lectures will be given by the following services: Gastric and Mixed Tumor, Bone, Thoracic, Radiology, Pediatrics, Chemotherapy, Gynecology, Head and Neck, Genito-Urinary, and Neurosurgical. The faculty will consist of 20 members of the

attending staffs of Memorial Hospital and Sloan-Kettering Institute for Cancer Research. The class will meet at 8:30 a. m. to 4 p. m. at Children's Pavilion, Memorial Center. The fee is $35. The class will be limited to 15 physicians.

For information address: Director, Pediatric Service, Memorial Center, 444 E. 68th St., New York.

Postgraduate Course on Heart Disease.—Doctors from all over the United States have been invited to attend an Armed Forces Institute of Pathology postgraduate course on diseases of the heart to be held in Washington, D. C., from May 14 to 17.

The course, which will deal with heart diseases from various clinical aspects as well as the pathologic viewpoint, is another service of A.F.I.P., the central laboratory of pathology for the Armed Forces.

This study will enable the physician to acquire a better understanding of the pathology of heart disease, thereby aiding him in diagnosing and treating his patient.

The symposium, according to Dr. William C. Manion, Chief of A.F.I.P.'s cardiovascular section and course director, is designed to familiarize the clinician as well as the pathologists with the problems of heart disease and to acquaint him with the recent advances made in this field.

The four-day course will be open to a total of four hundred twenty-five civilian and armed services physicians. Civilian physicians who desire to attend may apply to the Director, Armed Forces Institute of Pathology, Washington 25, D. C. Doctors in the armed forces should apply through normal military channels.

Participants in the symposium will include: Dr. Bradley M. Patton, University of Michigan; Dr. Oscar V. Batson, University of Pennsylvania; Dr. Maurice Lev, Miami; Dr. Edward Hawthorne, Howard University; Dr. Theodore Koppanyi, Georgetown University; Dr. Jesse E. Edwards, Mayo Clinic; Col. Thomas Mattingly, Walter Reed Army Hospital; Dr. T. F. Hilbish, National Institutes of Health; Dr. Charles Hufnagel, Georgetown University; Dr. T. G. Borilla, Walter Reed Army Medical Center; Dr. Proctor Harvey, Georgetown University; Major John Maloney, A.F.I.P.; Major Edward Jahnke Jr., Walter Reed Army Medical Center, and Dr. Otto Saphir, University of Illinois.

Also taking part will be Dr. Charles Friedberg, Columbia University; Dr. Joseph T. Roberts, Buffalo Veterans Administration Hospital; Col. Byron Pollock, Fitzsimons Army Hospital; Dr. Walter C. Putschar, Charleston General Hospital; Dr. Henry Swan, Denver; Dr. Sylvester E. Gould, Wayne County General Hospital; Dr. Kenneth R. Mallory, Boston City Hospital; Dr. Frank Johnson, A.F.I.P.; Lieut. Col. Loren F. Parmley Jr., Walter Reed Army Medical Center; Dr. Richard Follis, A.F.I.P.; Dr. Samuel Rosen, A.F.I.P., and Dr. William Von Glahn, Louisiana State University Hospital.

Short Courses.—The following short courses will be conducted at The Children's Hospital of Philadelphia in May and June 1956.

Pediatric Advances for Pediatricians and General Practitioners.—May 28 through June 1, 1956. A Refresher Course conducted by the Staff of the Children's Hospital of Philadelphia, in collaboration with the Department of Pediatrics of the University of Pennsylvania and the Camden Municipal Hospital. Tuition, $100.

Practical Pediatric Hematology.—June 4, 5, and 6. Conducted by Dr. Irving J. Wolman and other members of the Hematology Department of the Children's Hospital, under the auspices of the Graduate School of Medicine, University of Pennsylvania. Tuition, $60.

Blood Group Incompatibilities and Erythroblastosis Fetalis.—June 7 and 8. Conducted by Dr. Thomas R. Boggs Jr. of the Philadelphia Serum Exchange of the Children's Hospital of Philadelphia, under the auspices of the Graduate School of Medicine, University of Pennsylvania. Tuition, $50.

For information write to Irving J. Wolman, M.D., Children's Hospital of Philadelphia, 1740 Bainbridge St., Philadelphia 46.

Books

BOOKS RECEIVED

Les Gamma-globulines et la médecine des enfants. Edited by Raymond Gautier. Price, 2000 francs. Pp. 298, with 62 illustrations. Masson & Cie, 120 boulevard Saint-Germain, Paris, 6e, 1955.

La Rieducazione motoria delle paralisi cerebrali infantili. By A. Colli Grisoni. Price, not given. Pp. 194, with 38 illustrations. Casa editrice Licinio Cappelli, Via Farini, 6, Bologna, 1955.

Les Enfants difficiles. By Georges Amado. Price, 480 francs. Pp. 180. Presses universitaries de France, 108 Boulevard Saint-Germain, Paris, 6e, 1955.

Traitement des diarrhées du nourisson. By Jean Levesque. Price, 1100 francs. Pp. 164. Gaston Doin & Cie, 8 place de l'Odéon, Paris, 6e, 1955.

Die genuine Vitamin-D resistente Rachitis. Walter Swoboda. Price, $2.50. Pp. 80, with 12 illustrations. Verlag für medizinische Wissenschaften Wilhelm Maudrich, Spitalgasse 1 b, Wien IX, 1955.

Le Diabète infantile et juvénile. By Pierre Uhry and Paul Ducas. Price, 3200 francs. Pp. 488, with 15 illustrations. Masson & Cie, 120 boulevard Saint-Germain, Paris, 6e, 1955.

Scurvy as a Skeletal Disease. By H. J. Van Wersch, M.D. Price, not given. Pp. 365, with 182 illustrations. Dekker & Van De Vegt N. V., Utrecht-Nijmegen, Netherlands, 1955.

Deshidratación en el lactante. By E. Jaso Roldan and E. De Yturriaga. Price, not given. Pp. 270, with 104 illustrations. Sucesores de Rivadeneyra, S. A., Madrid, 1955.

Medical Research: A Midcentury Survey. Volumes 1 and 2. By Esther Everett Lape. Price, $15.00. Pp. 1505. Little, Brown & Company, 34 Beacon St., Boston 6, 1955.

Les Explorations biologiques en pédiatrie. By Claude Polonovski and Jean Colin. Price, 3900 francs. Pp. 498. Expansion Scientifique Française, Paris, 1955.

Biologische Daten für den Kinderarzt: Grundzüge einer Biologie des Kindesalters. Volumes 1 and 2. By Joachim Brock, Editor. Second edition edited by A. Adam and others. Price: Vol. 1, cloth, 73 marks; Vol. 2, cloth, 125 marks; 198 marks per set. Pp.: Vol. 1, 651, with 78 illustrations; Vol. 2, 1183, with 177 illustrations. Springer-Verlag, Reichpietschufer 20, (1) Berlin W. 35, 1954.

Poliomyelitis. Compiled and edited for International Poliomyelitis Congress. Price, $7.50. Pp. 567, with 442 illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5, 1955.

J. A. M. A. Clinical Abstracts of Diagnosis and Treatment. Edited by Noah D. Fabricant. Price, $5.50. Pp. 627. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1955.

Polio Pioneers. By Dorothy and Philip Sterling. Price, $2.75. Pp. 128, with numerous illustrations. Doubleday & Company, Inc., 575 Madison Ave., New York 22, 1955.

Rheumatoid Arthritis and Psoriasis Vulgaris. By Tibor Benedek, M.D. Price, $12. Pp. 308, with 57 illustrations. Chicago Medical Book Company, Jackson and Honore Sts., Chicago 12, 1955.

Psychoanalytic Study of the Child. Vol. 10. Edited by Ruth S. Eissler and others. Price, $7.50. Pp. 394. International Universities Press, Inc., 227 W. 13th St., New York 11, 1955.

Caring for the Sick Child at Home. By Marion Lowndes. Price, $3. Pp. 157. The Westminster Press, Witherspoon Building, Philadelphia 7, 1955.

Importance of Physiotherapy in the Treatment of Sick Children. By J. M. Jewry-Harbert. Price, $2.50. Pp. 84, with 15 illustrations. John de Graff, Inc., 64 W. 23d St., New York 10, 1955.

Splenin A in Rheumatic Fever. By Alvin F. Coburn, Judith Wood, Lucile V. Moore, and Mary Roberts. Price, $3.75. Pp. 87, with 5 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill., 1955.

Functional Otology: The Practice of Audiology. By Morris F. Heller, Ellis E. Singer, and Bernard M. Anderman. Price, $5.50. Pp. 225, with 31 illustrations. Springer Publishing Company, Inc., 44 E. 23d St., N. Y. 10, 1955.

The Pediatric Years. By Louis Spekter, B.S., M.D., M.P.H. Price, $12.50. Pp. 734, with 20 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill., 1955.

Community Programs for Mental Health. By Ruth Kotinsky and Helen L. Witmer. Price, $5. Pp. 362. Harvard University Press, Cambridge 38, Mass., 1955.

International Symposium: Cardiovascular Surgery. Edited by Conrad R. Lam, M.D. Price, $12.75. Pp. 543, with numerous illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5, 1955.

Ciba Foundation Symposium: Experimental Tuberculosis: Bacillus and Host. Edited by G. E. W. Wolstenholme and Margaret P. Cameron, assisted by Cecilia M. O'Connor. Price, $9. Pp. 396, with 69 illustrations. J. & A. Churchill, Ltd., 104 Gloucester Place, Portman Sq., London, W. 1, and Little, Brown & Company, 34 Beacon St., Boston 6, 1955.

Special Education for the Exceptional. Volumes 1, 2, and 3. Edited by Merle E. Frampton and Elena D. Gall. Price, each $5.50. Vol. 1: Pp. 453, with 2 illustrations. Vol. 2: Pp. 677, with 22 illustrations. Vol. 3: Pp. 700, with 9 illustrations. Porter Sargent, Publishers, 11 Beacon St., Boston 8, 1955.

Atlas und kurzgefasstes Lehrbuch der Phonokardiographie und verwandter Untersuchungsmethoden. By K. Hollack and D. Wolf. Price, $11.80. Pp. 171, with 149 illustrations. Georg Thieme Verlag, Herdweg 63 (14a) Stuttgart N; American agent, Intercontinental Medical Book Corporation, 341 4th Ave., New York 16, 1956.

Differentialdiagnose innerer Krankheiten. By Dr. Robert Hegglin. Price, $16.55. Pp. 678, with 372 illustrations. Georg Thieme Verlag, Herdweg 63, (14a) Stuttgart N; American agent, Intercontinental Medical Book Corporation, 341 4th Ave., New York 16, 1956.

A. M. A. Scientific Exhibits, 1955. Sponsored by the Council on Scientific Assembly, American Medical Association. Price, $20. Pp. 784, with numerous illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1955.

Therapie der Kinderkrankheiten. By Josef Siegl. Price, $12. Pp. 432, with no illustrations. Verlag fur Medizinische Wissenschaften, Wilhelm Maudrich, Wien, 1953.

Physiology and Pathology of Infant Nutrition. Ed. 2. By L. F. Meyer and Erich Nassau. Price, $11.50. Pp. 533, with 59 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Sprinfield, Ill., 1955.

The Skin: A Clinicopathologic Treatise. By Arthur C. Allen. Price, $25. Pp. 1048, with 495 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1954.

Exploración clínica en pediatría. By A. Galdo and M. Cruz. Price, not given. Pp. 892, with 459 illustrations. Editorial Quesada Granada, Spain, 1955.

BOOK REVIEWS

The Skin: A Clinicopathologic Treatise. By Arthur C. Allen. Price, $25. Pp. 1048, with 495 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1954.

This book is a magnificent and monumental reference work which contains almost two thousand individual clinical and histologic illustrations. The unique experience of the author in general pathology and dermatopathology coupled with his broad scholarship has resulted in an invaluable source of detailed information presented in a clear refreshing fashion. Almost all known abnormalities of the skin are included, with about one-third of the book devoted to tumors. The author presents both sides of many controversial issues. In some instances, as in denying the existence of a true epidermal basement membrane or in insisting that the dendritic melanocytes are not the sole source of melanin pigment, he is probably on the losing side, but in an astonishing comprehension of a vast field he reveals detailed knowledge, as, for example, by questioning the viral etiology of aphthae. His therapeutic optimism, as in Plate 246, in which geographic tongue is reported to be improved by the administration of yeast, probably results from more experience at the microscope than in the clinic. To ascribe the postacne keloids of the chest in Plate 350 to the x-ray administered is undoubtedly misleading and untrue. Although there are some points on which authorities would disagree, the book has the unity and tight organization that comes from single authorship. As both an atlas and a reference text, it represents an outstanding publishing event. All physicians who see skin lesions, whether intact or through the microscope, should become familiar with and make use of this invaluable book.

Chronik der Kinderheilkunde. Ed. 2. By Albrecht Peiper. Price, 30 deutsche marks. VEB Georg Thieme, Hainstrasse 17/19 Aufg. C, Leipzig C. 1, 1955.

This history of pediatrics is a thorough guide of the medicine of children from prehistoric times to the present and the story of the gradual emancipation of pediatrics.

Every historic point connected with children and their development is well described, and this includes also the controversial history of the foundling hospitals, child clinics, sociology in childhood, and many more.

A few facts are worth mentioning, such as the tremendous impact child mortality must have had on the survival of the human race. As exhumations showed, the graves of children in prehistoric times amounted to about forty per cent of all graves. In the history of the foundling hospitals and homes in France in the seventeenth century, we find a mortality of ninety per cent in those institutions.

As far as education is concerned, the strict system, often with corporeal punishment, was advocated in the last century; still, they had juvenile delinquency too. Though alcoholic drinks are taboo for our youth below ten, about two hundred years ago wine and in some instances also beer were a part of the diet of children over three years of age.

A review of the history of the pediatric illnesses and their treatment showed among other things that the diphtheria mortality, like that in several other children's diseases, had dropped in the late eighties of the last century, before, for instance, the diphtheria serum had been used.

It would be endless to mention all the interesting points of this book, which, by the way, has many old illustrations and reproductions.

The only evident defect the book has is the lack of pediatric history and bibliography from the United States of America.

Clinical Pathologic Conferences of Cook County Hospital: Vol. 1. Cardiovascular-Renal Problems. Edited by Hans Popper and Daniel S. Kushner. Price, $5. Pp. 325, with numerous illustrations. McGraw-Hill Book Company, Inc., 330 W. 42d St., New York 36, 1954.

From Cook County Hospital will come a series of publications on selected topics of pathology and internal medicine. The current work, Vol. 1, includes a detailed analysis of 26 autopsied cases. The material is organized according to conventional clinical pathologic exercises and is divided into three sections: cardiac, vascular, and renal. Forty-two physicians from medical schools and hospitals in the Chicago area participate in the discussions.

Differential diagnosis and management of patients is treated in some detail, and pathologic presentations are well executed, with better than average plates. Recent scientific developments relating to the diseases described are mentioned. Four pediatric cases appear. These involve congenital and rheumatic heart disease, acute hemorrhagic nephritis, and nephrotic syndrome.

House officers and medical students, as well as internists and pathologists, should find this book of interest.

Unfortunately, the clinical pathologic conference as a medium does not lend itself to adequate coverage of relevant biochemical information. This constitutes the only major criticism of the book's teaching value.

Growth at Adolescence. By J. M. Tanner. Price, $6.50. Pp. 212, with 10 photographs and 57 figures. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill., 1955.

Since no adequate text has as yet been written on "growth and development," the author is to be commended for his work on the most important phase of this period. In fact, and as the author admits, his text extends backward to include the entire period of growth in many instances.

The importance of accurate interpretation of growth data is discussed. There is no question but that data of the longitudinal type gives the only real and accurate picture on growth findings, inasmuch as it will show the direction of growth.

Every muscular and skeletal dimension seems to take part in the adolescent spurt. The trend of these changes is depicted in graphic form. From the reproductive standpoint, the development of the penis, testes, uterus, ovaries, and prostate during adolescence is spectacular in its rapidity. This is well illustrated.

In discussing factors affecting the time and character of the adolescent spurt, the author mentions genetics as the most important. Others are physique, nutrition, health, secular trends, socioeconomic trends, and climate. He does not believe climate to be of much influence in this regard. This latter observation would not meet with agreement with those of us who have observed adolescence in southern Florida.

His discussion on physiological and endocrinological changes emphasizes the dearth of objective information which is available at this time.

In summation, Dr. Tanner has compiled and discussed the changes which accompany adolescence, using whatever knowledge is now at hand. The information is so detailed by necessity that I do believe it will be of great help to a teacher or research worker in this or related fields, though I doubt whether it will be of great interest to a medical student, except, perhaps, as an occasional source of reference.

Handbook of Pediatrics. By Henry K. Silver, C. Henry Kempe, and Henry B. Bruyn. Price, $3. Pp. 548. Lange Medical Publications, P. O. Box 1215, Los Altos, Calif., 1955.

This first edition of a very useful handbook for quick reference on pediatric subjects is well accepted by medical students and house officers. It is extraordinarily complete despite its small size.

The main objections are those applicable to any condensed handbook: (1) small print making for difficult reading, (2) a tendency for those in training to allow this publication to supplant more complete discussions, and (3) in order to secure brevity the necessary generalizations do not reflect the disparity in views of other authorities on some of the subjects.

Some sections are especially concise and complete, such as the one on chemotherapy and antibiotics. This handbook can be recommended as a quick source of useful information.

International Symposium, The Hypophyseal Growth Hormone: Nature and Actions. Edited by Richmond W. Smith, Oliver H. Gaebler, and C. N. H. Long. Price, $12. Pp. 576, with numerous illustrations. McGraw-Hill Book Company, Inc., 330 W. 42d St., New York 36, 1955.

This volume is a verbatim report of the proceedings of an international symposium attended by forty-five experts actively engaged in the investigation of the hypophyseal growth hormone (HGH). Groups of papers on various phases of the subject are presented and discussed.

Certain aspects of the bioassay and chemistry of HGH are covered. There is a comparative study of the hormone secreted by several species of animals. Effects of the hormone upon inflammation and upon the morphology and physiology of digestive glands, bones and joints, tissue cultures, and renal function are described. Evidence is presented that HGH can function in the presence of nutritional deficiencies. Various aspects of the metabolic effects of the hormone are discussed, with a great deal of attention being paid to the relationship between HGH and glucose metabolism.

In almost all of the material covered, animal studies are the source of information. However, the last two papers describe the effects of HGH on patients. Here most of the effects noted on animals can be demonstrated, although inconsistently and to a lower degree.

As a review of current thought and investigation in this as yet little-understood field, this volume is of great value. It is unusually well illustrated for this type of book.

Therapie der Kinderkrankheiten. By Josef Siegl. Price, $12. Pp. 432. Verlag fur Medizinische Wissenschaften, Wilhelm Maudrich, Wien, 1953.

This book is part of an encyclopedic medical book series, but can be acquired separately. It covers the therapeutics in respect to nutrition and growth and gives the latest in all medical and surgical therapeutics for the modern pediatrician.

Not only are drugs given, but hundreds of medical pediatric procedures and methods of healing are described in detail.

This book shows us again that though the antibiotics of the last ten years are a necessity, a great many pediatric conditions can be treated with a much simpler approach.

If it comes to prescription writing, this book offers an immense number of valuable formulas, with correct dosage in the decimal system. The book is excellently indexed. It is a fine contribution to pediatrics and is highly recommended.

Psychopathology and Education of the Brain-Injured Child. Vol. 2. By Alfred A. Strauss and Newell C. Kephart. Price, $6. Pp. 266. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1955.

This second volume, pertinent to problems of the brain-injured child, follows the style of most publications of the fundamentals, the treatment, and the management of the brain-injured child from the point of view of neuropediatrics. The authors admit freely to changes in theory of brain function and have posited a very basic and understandable concept. It is true that much more should be done in this field, and this volume goes further than the previous publication to enlarge upon the available knowledge of the brain-damaged child. It would be extremely wise of physicians, psychologists, and psychiatrists dealing intimately with the problem to read this book carefully. Basic information in anatomy, physiology, and embryology is well written, the psychopathology of the four major fields of investigation—perception, language concept and formation, and behavior—are discussed in terms of fundamentals. The outline of testing techniques is of great importance to psychologists and should be understood thoroughly by a neuropediatrician. The author's conclusions are tentative at best, and it will take many more years to understand completely many phenomena. Certainly the authors have made an excellent beginning at uncovering essential data regarding the brain-damaged child. Pertinent cases are cited and add considerably to the informative value of this interesting text.

Congenital Malformations and Birth Injuries: A Handbook on Nursing. By Jessie Stevenson West, R.N. Price, $1. Pp. 178. Association for the Aid of Crippled Children, New York, 1954.

A handbook on nursing of congenitally deformed and birth-injured children is a timely contribution, since the mortality of defective children has been reduced in recent years by surgical and hygienic measures and many children are kept alive who previously would have died soon after birth. Such children require special nursing care as well as psychological and social integration into their environment. This small book offers an intelligent and understanding introduction to the field. Two general chapters deal with basic questions of the origin and incidence of malformations and with nursing responsibilities. Special chapters are devoted to orthopedic problems, such as congenital torticollis, dislocation of the hip, and club foot. Malformations of the heart, of the gastrointestinal tract, and of the urogenital system and defects of the eye and of the ear are also discussed. A guide for nursing observation of infants and children is added, and the responsibilities of the nurse in the early recognition of congenital defects are stressed. The nursing problems posed by the various anomalies and the need for prevention of complications are adequately discussed. The situation of the parents and their need for reassurance, guidance, and counseling are pointed out. Appended to each chapter is a list of useful references. Especially noteworthy is the section on cerebral palsy, which is followed by a list of more than forty pertinent articles. Although the book is written for nurses, it can be recommended also to

physicians, medical students, and parents. The Association for the Aid of Crippled Children, which is sponsoring many projects in the area of congenital malformations, has made another valuable contribution by publishing this book at a reasonable price.

Moderne Probleme der Pädiatrie (Modern Problems in Pediatrics; Problèmes actuels de pédiatrie). By A. Hottinger and F. Hauser. Price, 60 Swiss francs. Pp. 816, with 180 illustrations. S. Karger AG., Arnold Böcklinstrasse 25, Basel, 1954.

The purpose of this volume is to present a cross section through the problems of modern pediatrics and to foster contact between research worker, obstetrician, and pediatrician. There are eighty-eight separate contributions on pediatric subjects, arranged in such sections as prenatal diseases, perinatal mortality, prematurity, nutritional disturbances, metabolism, allergy, infectious diseases, and hematology. The selection of articles covers a wide field of the current important problems of pediatrics. One hundred twenty-seven authors from different countries, many of them from Switzerland, have contributed articles, written in either German, French, or English. Translated summaries are added. Each author writes on subjects in which he is a recognized authority.

J. Warkany discusses prenatal diseases and arrives at the following conclusions: "The field of prenatal pathology is a no man's land at the present time. To cultivate it, close cooperation between obstetricians and pediatricians is required. Biology, embryology, and genetics, sciences not sufficiently consulted by pediatricians in the past, must be incorporated into the prenatal pediatric research."

Clement R. Smith, in a very stimulating article, discusses perinatal mortality. An interesting contribution by T. H. Koller and P. Erb deals with the problem of Caesarean section and its influence on the prognosis of the newborn. Various aspects of prematurity are discussed by W. Tobler (modern nursing care), H. H. Gordon (retrolental fibroplasia), and O. Jirovic (interstitial pneumonia due to pneumocystis carinii). In the following sections, E. Berger reports on observations on pathogenic colon bacilli, H. F. Helmholz on fluoridation for all children, D. C. Darrow on parenteral fluid therapy, and E. Polacek on the same subject. Other articles in the field of metabolism deal with proteins, amino acids, vitamins, and hormones. Among the papers on infectious diseases, the following may be mentioned: immunophoresis (Stokes Jr. and I. Smolens), poliomyelitis (A. B. Sabin), Coxsackie virus (W. Keller), and cat-scratch fever (R. Debré). A. Wallgren discusses complications of primary tuberculosis, S. van Creveld, recent advances in hemorrhagic disorders.

This brief selection of articles may indicate the scope of the volume. It is impossible to give due credit to the many other interesting contributions. It seems to the reviewer that this is a collection of very stimulating papers which reflects the spectacular progress in modern pediatrics as well as the brilliant work which is being devoted to the many still unsolved problems.

The book is a fine dedication to the seventieth birthday of Professor Freudenberg and gives testimony of the high standard of pediatrics in his country.

Die moderne Behandlung der Poliomyelitis im akuten Stadium. Edited by Prof. Dr. G. Fanconi. Price, $2. Pp. 71, with 19 illustrations. Benno Schwabe & Co., Basel 10; American agent, Intercontinental Medical Book Corp., New York, 1954.

This book is a compilation of a series of papers presented at a meeting in Switzerland in June, 1954, under the direction of Prof. G. Fanconi, Director of the Children's Hospital in Zurich. The major theme was a consideration of artificial respiration in the life-threatening forms of poliomyelitis.

Practical demonstrations of the newer methods and the theorectical considerations for their use were presented. The subjects were as follows:

(1) Short introduction to the physiology and pathophysiology of respiration with special regard for artificial breathing.
(2) The management of life-threatening poliomyelitis.
(3) Respiratory problems concerned with life-threatening paralysis of breathing.
(4) Technique in management of insufficient respiration in acute poliomyelitis.
(5) Respiratory physiology observed in artificial breathing in the management of tetanus.
(6) Modern management of severe tetanus.
(7) Desire and reality in the management of poliomyelitis in the Children's Hospital, Zurich.

In the various articles there is a discussion of electrolytes, O_2 and CO_2 relationships, the significance of blood-pressure determinations, and respiratory acidosis and alkalosis, all by way of introduction to the proper use of the tank and cuirass respirators.

The second paper, by Neukirch, and the third, by Engstrom, are particularly well written. They discuss in detail the management of the various types of poliomyelitis, the problem of suction, aspiration, tracheotomy, and the use of respirators. The ideas expressed are in agreement with practices in this country.

A discussion of tetanus was introduced apparently to correlate the principles used in therapy with those in use in poliomyelitis.

Fanconi, in the final paper, has summarized the general treatment of poliomyelitis, both acute and chronic, in all of its phases. There is a plea made for special centers for the management of patients ill with the disease.

For those concerned with management of the severe forms of poliomyelitis, this series of papers will be of especial interest.

Counseling in Medical Genetics. By Sheldon C. Reed. Price, $4. Pp. 267. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5, 1955.

This is a very welcome monograph that should get wide circulation. Dr. Reed's thesis is that physicians are being asked questions continually that bear on genetics but that all too few physicians are informed in this field. Having come to the conclusion that physicians should be better informed regarding genetics, Dr. Reed has gone a good step farther by writing a very readable book which this reviewer found hard to put down until it was finished. The most important genetic problems have been covered in short chapters on Mongolism, cleft palate, congenital heart disease, blood genetics, including disputed parentage, and allergies, to name a few. There is also an appendix consisting of brief listing of the inheritance of some one hundred fifty conditions.

The text is authoritative but written in an easy style. This book should be required reading for all physicians, such as pediatricians and obstetricians, who might counsel with families about problems of heredity. Fortunately, such a requirement would be a pleasure.

Prolonged and Perplexing Fevers. By Chester S. Keefer and Samuel E. Leard. Price, $5.50. Pp. 248. Little, Brown & Company, 34 Beacon St., Boston 6, 1955.

This monograph consists of two main parts. The first is a very good discussion of heat products and heat regulation that serves as an excellent background for a consideration of the factors in addition to disease that may give rise to elevated temperature. The variations of temperature in health are stressed, and the reader is cautioned against considering all "fever" as pathologic.

The second part of the book consists of a series of chapters on various obvious and obscure illnesses associated with fever. The most important subjects listed are tuberculosis, sepsis, both local and generalized, tumors, and the collagen diseases. Numerous case histories are used to illustrate salient points. This section was somewhat disappointing, since it did not give an orderly approach to diagnosis. The fact that practically all of the material deals with adults makes it less valuable for physicians working with children. The references are excellent.

Die Bedeutung der frühkindlichen Hirnschädigung für die Kinderpsychiatrie. By Dr. Gerhard Göllnitz. Price, not given. Pp. 149. VEB Georg Thieme, Hainstrasse 17-19 Aufg. C, Leipzig C 1, 1954.

This book stresses the significance of the infantile brain damage also called encephaloperoma infantis on the child psychiatry. With exception of the small number of psychoses in children, the author demonstrates that there is not a chapter in child psychiatry which is not dominated in the psychic and somatic sphere by an encephaloperoma infantis. Since physicians are now able to diagnose without serious intervention the most intricate disturbances in function and development in the infantile cerebrum, they can distinguish between inherited disturbances in intelligence and personality and those due to brain damage in the infant. It could be demonstrated that most disturbances are acquired and due to encephaloperoma infantis and that the latter is also severer than the inherited form. The brain damage occurs in the earliest infancy or childhood and can be proved by encephlography, which shows the same results as the anatomical findings of many other authors. In addition to this the author succeeded in working out in analogy with the

traumatic cerebral weakness of the adult also a specific form of cerebral weakness due to infantile brain damage. The special distinction is that the age of the child is correlated with the symptomatology. Additionally we have to consider the external influences to which the child is more liable.

All the above results changed the prognosis and therapy in child psychiatry. In addition to the old pedagogic procedures the author advocates aimed motor treatment and glutamic acid. The book has an appendix with many clinical cases and a motometric scale of Oseretzky.

Deutsche Nachkriegskinder. Edited by C. Coerper, W. Hagen, and H. Thomae. Price, 33 Deutsche marks. Pp. 545, with 92 illustrations. Intercontinental Medical Book Corp., New York 16, 1954.

The number of co-workers is given as twenty-seven, with assistance of nineteen more. Aided by the Marshall Plan, a comprehensive study was undertaken with the view to correlate various factors of somatic and psychic growth and development, including such environmental conditions as family and social situation. The studies were carried out in six different localities. The intention was to follow a certain number of children from entrance to grade school to graduation from grade school; that is, boys and girls from about six to fourteen years of age. At this time only the results of the first year (1952), based on 4400 children, were available, the majority of which necessarily belonged to the school-entrance group. The group of workers in each locality consists of a physician, a psychologist, and a welfare worker, with their assistants. Uniform methods of examination and tests were adopted. The procedures are given in detail in the first part of the book, in 229 pages. The second part, of 301 pages, deals with the results of the examinations. It is fully recognized that at present it is only possible to give indications of the trend of longitudinal development. A chapter is devoted to "habitus" diagnosis. Habitus delineates the present appearance (phenotype), when the form is looked upon as the result of the development, that is, as "formed function," allowing insight into the peculiarities of the individual. It does not mean constitution. With due apology to the authors, an appropriate verse of Wilhelm Busch may be cited, "So gilt doch dies Gesetz auf Erden—wer mal so ist muss auch so werden," meaning, in a less ponderous language, that the present state of an individual derives from its antecedents.

Since it is not in general use the "physiognomy" test of Thomas may be mentioned, one of the psychological tests. A series of pictures of heads are laid before the person to be tested, who is asked to arrange them according to various features portrayed. Children, at the age of dismissal from grade school, are subjected to a graphological test.

In a postscript the editors summarize eight permissible conclusions. Of these it may be mentioned that bad or good environmental conditions do not exercise necessarily good or bad effects on somatic or psychic development. It was not possible to establish statistically significant correlations between somatic and psychic "habitus." It cannot be affirmed that the tempo of somatic and psychic development keep pace together in the same individual. Somatic and psychic changes appear to a large extent as independent variables. Even if in places a greater economy of words might be coupled with greater clarity, the book contains so much of interest that such and other minor faults can be overlooked.

The Management of Mental Deficiency in Children. By I. Newton Kugelmass. Price, $6.75. Pp. 312. Grune & Stratton, Inc., 381 4th Ave., New York 16, 1954.

Mental deficiency, once regarded as a homogeneous entity, now is recognized as a pattern of defective behavior that may be induced by any one of a large number of underlying disorders. The syndromes identified are so many and their etiology as yet sufficiently obscure that the task of classification presents a major challenge. The text under review, which arranges a copious amount of clinical material in a new scheme proposed by the author, fails to meet this challenge adequately.

Dr. Kugelmass suggests a quadripartite division into "developmental, metabolic, neuromotor, and psychological amentia." These categories lack a common point of reference—etiologic, anatomic, or clinical—and consequently are neither logically exhaustive nor sufficiently inclusive. Developmental metabolic disorders, such as phenylketonuria, must therefore be arbitrarily assigned one or the other rubric. "Metabolic" is forced to suffice for diseases as different as juvenile neurosyphilis and Niemann-Pick's disease. It is difficult to fathom what use of the term "psychological" can justify the inclusion within its province of processes like cerebral palsy, the encephalopathies and encephalitides, malnutrition, and hypoglycemia.

The book is strongest in its clinical sections and weakest in its theoretical chapters. The author indulges, on the one hand, in fanciful "neurologizing" without experimental basis and, on the other, seems oblivious of the sociological contributions to an understanding of the problem of relative mental deficiency. The problems in psychometric testing, the influence of cultural deprivation on test scores, and the nature of the limited correlation between score and academic performances are given insufficient attention. It is distressing to find the author stating "Hippocrates considered seizures sacred" (p. 149). On the contrary, the Hippocratic school made a classical contribution to the progress of medical science by its insistence that "the disease (epilepsy) is no more divine than any other. . . . Men think it divine merely because they do not understand it. But if they called everything divine which they do not understand, why, there would be no end of divine things."

The inadequacy of the scheme of classification, the dogmatism and inaccuracy of the theoretical sections, and the many errors of fact, make it impossible to recommend this book for the pediatrician; the specialist in mental deficiency may find it provocative as well as provoking.

Genetica medica. Edited by Prof. Luigi Gedda. Price, 5000 lire. Pp. 468, with 170 illustrations. Edizioni dell'Istituto Gregorio Mendel, Piazza Geleno 5, Rome, 1954.

This well-printed and profusely illustrated volume contains the papers presented at the First International Symposium of Medical Genetics, which met in Rome, on Sept. 6 and 7, 1953. The symposium was held on the occasion of the dedication of the Gregor Mendel Institute of Medical Genetics and was attended by outstanding medical geneticists of many countries.

Thirty scientific communications are presented, preceded by the text of an address to the symposium by His Holiness, Pope Pius XII. Some of the scientific papers report the results of research, while others summarize broader areas. The papers are generally of excellent quality and cover such a wide range of diseases that they cannot be reviewed in detail here. Two of the papers are by Americans, F. J. Kallmann (mental disorder) and R. M. Stecher (joint disease). Outstanding among the summaries of the present status of genetic knowledge in specific fields are those on the detection of asymptomatic carriers of genetic disease, by Franceschetti and Klein, on endocrine disturbances, by Lehmann, on skeletal diseases, by Grebe, and on hemolytic disease of the newborn, by Mollison. Of the thirty papers included, five are in English, sixteen in Italian, seven in German, and two in French. Most of the papers are summarized in English. There is a detailed subject index. This volume is highly recommended to those interested in genetic factors in disease.

The Adult-Child Interaction Test: A Projective Test for Use in Research. By Theron Alexander. Price, not given. Pp. 40, with 8 illustrations. Child Development Publications of the Society for Research in Child Development, Inc., 1341 Euclid, Champaign, Ill., 1955.

The adult-child interaction test is a picture story-telling test given individually or in groups and has been used on subjects between the ages of six and sixty-five years. The subject is instructed to tell a story about eight individual cards: what is going on in the picture, what has brought about the situation, and what the outcome will be. The cards portray situations involving children and adults.

The test is planned to give information about the adult's perception of children and vice versa. The pictures vary from other tests for children inasmuch as they show adults and children together, and this may well turn out to be an advantage. The author hopes it will also be useful in studying attitudes of the subject toward authority, toward sex, and toward relationships within the family.

An attempt is made at some objective scoring, and the author states he is working to put the results on a punch-card system. In its present form the interpretation depends very much on the experience of the examiner with this kind of test technique. The protocols of a child and of a teacher are presented and the findings compared with psychotherapeutic interviews with the former and observational data on the latter, studying the reaction of the teacher to children's behavior. The test is in its early stages of development, and, as indicated by the subtitle, it is published to stimulate further research on the technique. For the present it should therefore be handled by skilled psychologists with the aim of gathering research data rather than using it for service.

"Prompt healing without infection resulted in all traumatic lesions treated"*

". . . Furacin is an effective antibacterial drug which may be safely prescribed for a variety of conditions involving the external eye and lids."

[*BRENNAN, J.W.: AM. J. OPHTH. 35:1349, 1952.]

- rapid, effective antibacterial action against a wide variety of gram-negative and gram-positive organisms with unique lack of irritation
- does not inhibit phagocytosis or retard regeneration of the highly sensitive corneal epithelium
- effective in the presence of pus and mucus
- indicated in external ophthalmic bacterial infections including conjunctivitis, blepharitis, dacryocystitis, keratitis, hordeolum, lid abscesses and for the prevention of post-operative infections

FURACIN®
ophthalmic

FURACIN OPHTHALMIC LIQUID *(sterile) contains Furacin (brand of nitrofurazone) 0.02% dissolved in an isotonic aqueous solution. Dropper bottle of 15 cc.* FURACIN OPHTHALMIC OINTMENT *contains Furacin (brand of nitrofurazone) 1% in a petrolatum base. 3.5 Gm. tube.*

For infections of the nose and ear:

FURACIN nasal—topically effective antibacterial in rhinitis, nasopharyngitis and sinusitis: available in 15 cc. dropper bottles, providing Furacin (brand of nitrofurazone) 0.02% in an isotonic, buffered solution as: FURACIN NASAL WITH EPHEDRINE (with ephedrine•HCl 1%); FURACIN NASAL WITH NEO-SYNEPHRINE† (with phenylephrine•HCl 0.25%).

FURACIN ear solution—prompt antibacterial and deodorizing action in otitis.

FURACIN EAR SOLUTION contains Furacin (brand of nitrofurazone) 0.2% in hygroscopic, water-soluble, polyethylene glycol. Dropper bottle of 15 cc.

†NEO-SYNEPHRINE—REG. TRADEMARK WINTHROP-STEARNS, INC., BRAND OF PHENYLEPHRINE.

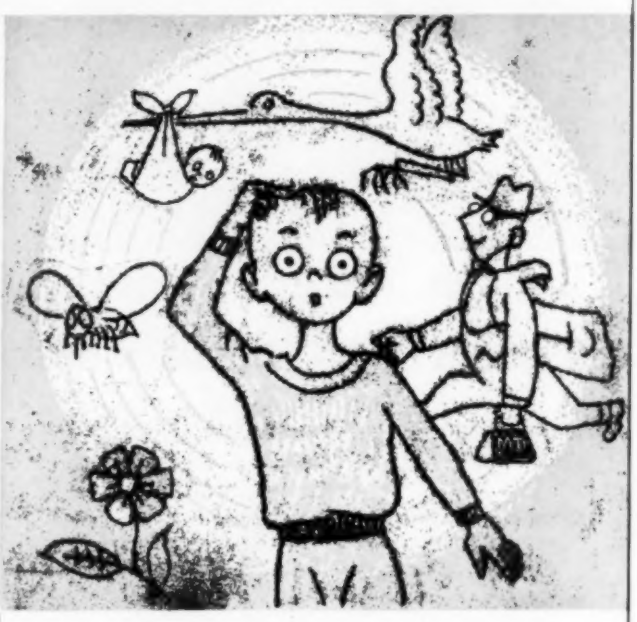
EATON LABORATORIES, Norwich, N.Y. **NITROFURANS** a new class of antimicrobials neither antibiotics nor sulfas

A NEW SERIES IN

SEX EDUCATION

Titles in the new series

- PARENTS' PRIVILEGE
  for parents of young children of pre-school and early school age
- A STORY ABOUT YOU
  for children in grades 4, 5, and 6
- FINDING YOURSELF
  for boys and girls of approximately junior high school age
- LEARNING ABOUT LOVE
  for young people of both sexes (about 16 to 20 years of age)
- FACTS AREN'T ENOUGH
  for adults who have any responsibility for children or youth that may create a need for an understanding of sex education



PRICES

Note: Discounts apply to quantities of any single title, or to quantities of sets.

Quantity	Discount	Price
1	—	$ .50
10	10%	4.50
25	30%	8.75
50	40%	15.00
100	50%	25.00
1000	60%	200.00

Set of 5 titles, $2.25.

Distributed By

Order Department

AMERICAN MEDICAL ASSOCIATION

535 N. Dearborn St.

Chicago 10, Ill.

ORDER BLANK

Enclosed is $_____(no stamps) for the following pamphlet(s):

Title	Quantity
1. PARENTS' PRIVILEGE	
2. A STORY ABOUT YOU	
3. FINDING YOURSELF	
4. LEARNING ABOUT LOVE	
5. FACTS AREN'T ENOUGH	
Complete set of five	

Please send pamphlet(s) to:
(Please Print)

Name_____

Street_____

City_____

Zone_____ State_____

CD 4-56

to reduce complications in the first year of life

SIMILAC®

a source of nutritional protection against infantile eczema...

▪ Linoleic and other unsaturated fatty acids believed to play an important role in the prevention and therapy of infantile eczema[1-4] are present in Similac, in amounts at least equal to those reported for breast milk.[5]

▪ Similac, in recommended quantities, provides protein closely approximating the physiologic level supplied by breast milk.[6] The fluidity of Similac protein, comparable to that of breast milk protein, assures rapid and complete digestion.[7] There is thus virtually no likelihood that products of incomplete digestion will be absorbed to cause an allergic eczematous reaction. In contrast, customary cow's milk mixtures are believed to deliver excessive amounts of protein, some of which cannot be completely digested and may be absorbed to cause a vascular reaction in the upper corium.[8]

there is no closer equivalent to the milk of healthy, well-nourished mothers

SUPPLIED: as Powder in tins of 1 lb., with measuring cup; as Liquid in tins of 13 fl. oz.

1. Editorial: J.A.M.A. *134*:606 (June 14) 1947. 2. Hansen, A. E., and Burr, G. O.: J.A.M.A. *132*:855 (Dec. 7) 1946. 3. Hansen, A. E.: Knott, E. M.; Wiese, H. F.; Shaperman, E., and McQuarrie, I.: Am. J. Dis. Child. *73*:1 (Jan.) 1947. 4. Hansen, A. E.: In Vitamin B_6 in Human Nutrition, Report of the Tenth M & R Pediatric Research Conference, Columbus, M & R Laboratories, 1954, p. 51. 5. National Research Council: Maternal Nutrition and Child Health, Bull. 123 (Nov.) 1950. 6. Meyer, H. F.: Essentials of Infant Feeding for Physicians, Springfield, Illinois, Charles C. Thomas, 1952, p. 44. 7. Martin, C. W.: New York State J. Med. *32*:1012 (Sept.) 1932. 8. Stoesser, A. V., and Nelson, L. S.: Journal Lancet *73*:687 (Dec.) 1953.

SCIENCE IN NUTRITION RESEARCH

ROSS LABORATORIES COLUMBUS 16, OHIO

*Specially processed non-diastatic malt extract neutralized with potassium carbonate. In 8 oz. and 16 oz. bottles.

Send for Samples and Literature

For HARD, DRY STOOLS OF CONSTIPATED BABIES

Borcherdt

MALT SOUP Extract*

A gentle laxative modifier of milk. One or two tablespoonfuls in the day's formula—or in water for breast fed babies—produce a marked change in the stool.

SAVES DOCTOR'S TIME, TOO!

Fewer phone calls from anxious mothers. Malt Soup Extract is merely added to the formula. Prompt results. Easy for mother to prepare and administer. Does not upset the baby.

BORCHERDT MALT EXTRACT CO.

217 N. Wolcott Ave. • Chicago 12, Ill.

Pancreatin

VIOKASE

NOT *enteric coated*

An accepted clinically effective* preparation in the treatment of disorders due to pancreatic insufficiency.

*Shwachman, H., Children's Hospital, Boston, The Child in Health and Disease, Gruloe and Eley, 2nd Edit.

Butler, A., Harvard Medical School, private communication.

Royce, S., Los Angeles Hospital, private communication.

Clay, W. A., Frank, D. W., and Logan, V. W., Studies on the Therapy of Pancreatic Insufficiency, Gastroenterology, 26: 169, 1954.

Everson, T. C., Grossman, M. I., and Ivy, A. C.: Bulletin of Amer. College of Surgeons, January, 1950.

Gibbs, G. E., Bradley, J. E., and Minor, J. V., Diagnosis and Treatment of Cystic Fibrosis of the Pancreas, J.A.M.A. 145: 1187 (1951).

Write for Literature

VioBin CORPORATION

MONTICELLO, ILLINOIS

BOOKLETS ON MENTAL HYGIENE

Here are several booklets on mental hygiene that may prove of interest and use to you and your patients.

EMOTIONAL HEALTH IN WORK AND PLAY. T. R. Retlaw. 8 pages. 15 cents.

MESMERISM MINUS MESMER. Stefan Zweig. A discussion of hypnotism. 5 pages. 5 cents.

JOE'S NERVOUS BREAKDOWN. John E. Eichenlaub. 6 pages. 10 cents.

YOUR STAKE IN MENTAL HEALTH. George S. Stevenson. 4 pages. 10 cents.

WHERE MENTAL PATIENTS RULE THEMSELVES. Murray Teigh Bloom. 4 pages. 10 cents.

Keep a supply of these booklets on hand. Available at lower cost for quantity purchases.

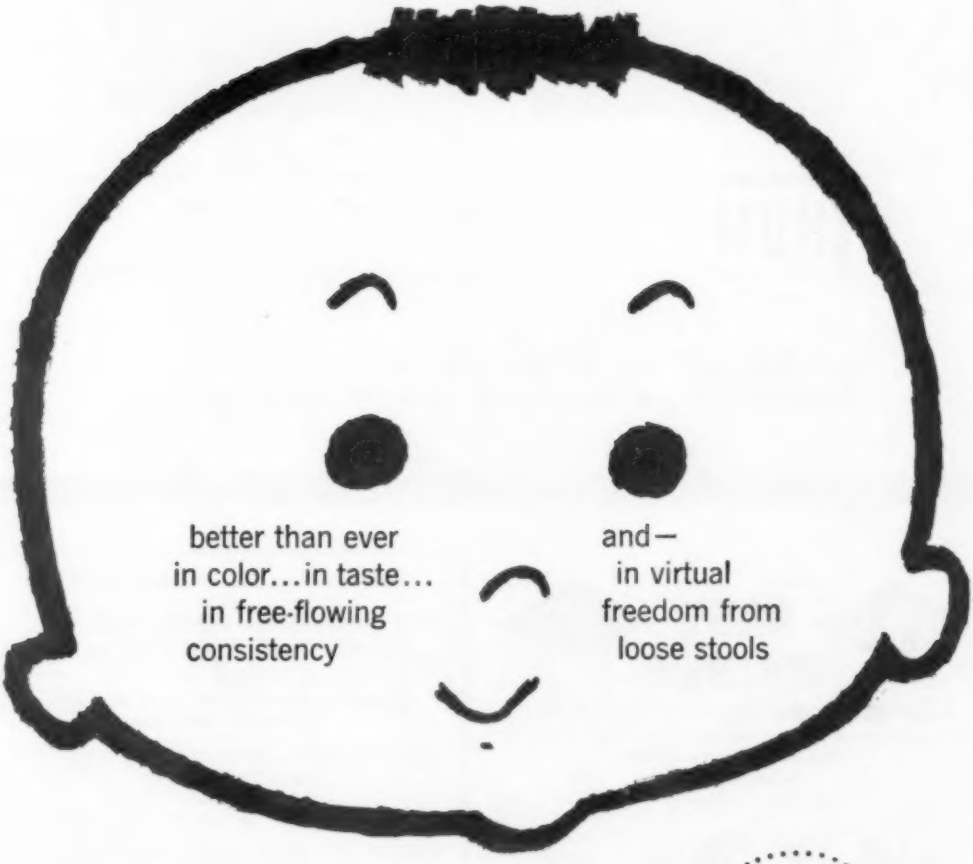
AMERICAN MEDICAL ASSOCIATION

535 North Dearborn Street

Chicago 10, Illinois

after 20 successful years
raising milk-allergic children...

better than ever



MULL-SOY®

Liquid TODAY

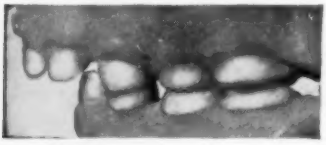
Thoroughly modern for modern tastes...yet *proved by time* as an effective hypoallergenic replacement for cow's milk whenever milk allergy is encountered or anticipated.

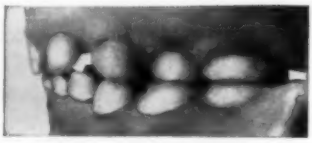
Available in 15½-fl.oz. tins. Start with 1:3 dilution with water, strengthen gradually to 1:1. Add carbohydrate and vitamins as required, at your discretion. Also available: MULL-SOY Powdered in 1-lb. tins at all drug outlets.

Borden's® PRESCRIPTION PRODUCTS DIVISION
350 Madison Avenue, New York 17

THUMBSUCKING

since infancy caused this 4 year old's malocclusion.





THUM
TRADE MARK

THUM broke the habit and teeth returned to normal position in 9 months.

THUM DISCOURAGES NAIL BITING TOO

GET THUM AT YOUR DRUGGIST OR SURGICAL DEALER.
PRESCRIBED BY PHYSICIANS FOR OVER 20 YEARS.

INVALEX **BABY WALKER** INVALEX

A PERFECT HELPER FOR THE 4 TO 8 YR. OLD

ALSO AVAILABLE IN JUNIOR & ADULT SIZES

PADDED BALANCE RING

LOCKS SECURELY IN PLACE

ADJUSTABLE IN HEIGHT AND POSITION

LARGE PADDED SEAT ON REAR

RUGGED EASY ROLLING CASTERS

CHROME SATIN OR BROWN ENAMEL FINISHES REMOVES ALL CLINICAL APPEARANCES

STRONG TUBULAR STEEL CONVENIENTLY LIGHT

MAXIMUM SECURITY AND COMFORT

INVALEX **INVALEX SALES CO., INC.**
741 WEST 17TH ST. LONG BEACH, CALIF.

THE PEDIATRIC DEPARTMENT
of
MEMORIAL CENTER FOR CANCER AND ALLIED DISEASES

announces that

The annual comprehensive three day course in Pediatric Oncology
for
PEDIATRICIANS, GENERAL PRACTITIONERS, HEALTH OFFICERS
will be held
April 25, 26 and 27, 1956

PURPOSE: To review current concepts regarding the neoplastic diseases of children particularly as to diagnosis, differential diagnosis and management, and to indicate the importance of the clinician's role in the control of cancer in childhood.

METHOD: Case demonstrations, clinics, lectures given by the following Services: Gastric and Mixed Tumor, Bone, Thoracic, Radiology, Pediatrics, Chemotherapy, Gynecology, Radiology, Head and Neck, Genito-Urinary, and Neurosurgical.

FACULTY: Twenty members of the Attending Staffs of Memorial Hospital and Sloan-Kettering Institute for Cancer Research.

TIME: 8:30 a.m. to 4 p.m.

PLACE: Children's Pavilion, Memorial Center

FEE: $35.00 Class limited to 15 physicians.

For information address:

DIRECTOR, PEDIATRIC SERVICE
MEMORIAL CENTER
444 EAST 68th STREET NEW YORK, NEW YORK

*VARAMEL

3 EASY STEPS

+ carbohydrate

+ water

*Made from Grade A Milk (U.S. Public Health Service Milk Code) which has been modified by replacement of the milk fat with animal and vegetable fats and by the addition of synthetic vitamins. No carbohydrate has been added.

THE BAKER LABORATORIES, INC.

Milk Products Exclusively for the Medical Profession

Main Office: Cleveland 3, Ohio • Plant: East Troy, Wisconsin

to help you combat iron deficiency in infants...

How Fer-In-Sol improved infants' blood pictures

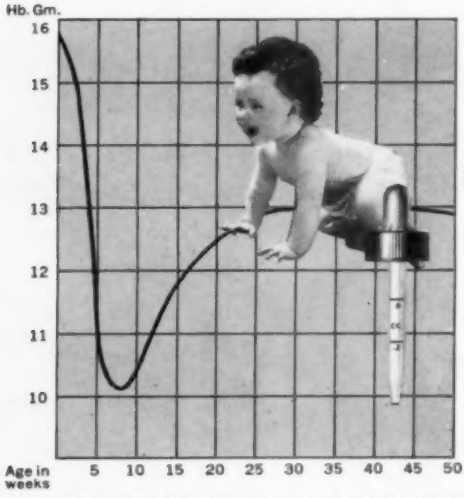


Chart adapted from Niccum, Jackson and Stearns: A.M.A. Am. J. Dis. Child. 86: 553, 1953.

Mean hemoglobin determinations of infants on a predominantly milk diet receiving Fer-In-Sol. The Fer-In-Sol dose was 5 mg. of iron (0.2 cc.) per day at 3 months, increased to 10 mg. of iron (0.4 cc.) after 6 months of age.[1]

Fer-In-Sol

iron in a drop for infants and children

"Iron deficiency anemia has a peak incidence between six months and two and one-half years..."[2]

Smith and Rosello[3] found that the peak incidence of iron deficiency in infants and children occurred between the ages of 6 and 24 months, when growth is most rapid. Sturgeon[4] reports that published data indicate iron deficiency in infants is common. Although consuming normal diets, the majority of infants in the last half of the first year of life, and throughout the second year of life, "exist in relatively severe states of iron deficiency (30% or more depleted)."[4]

Niccum, Jackson and Stearns[1] found that prophylactic administration of Fer-In-Sol in small daily doses "was sufficient to maintain hemoglobin values at a constant level throughout the latter half of infancy in all full term infants"... resulted in significantly higher hemoglobin values than did ferric ammonium citrate.

FER-IN-SOL

Fer-In-Sol® provides a pleasant way to supply ferrous sulfate—a well tolerated, well absorbed and efficiently utilized form of iron. The vehicle is acidulous to improve absorption and utilization. The good taste of the solution makes it readily acceptable to young children. And tolerance is good.

Only 0.3 cc. of Fer-In-Sol supplies 7.5 mg. of iron—more than the Recommended Daily Allowance for children up to 4 years old. Fer-In-Sol is supplied in 15 cc. and economical 50 cc. bottles, with the new calibrated 'Safti-Dropper' of unbreakable plastic.

(1) Niccum, W. L.; Jackson, R. L., and Stearns, G.: A.M.A. Am. J. Dis. Child. 86: 553, 1953. (2) Smith, C. H.: Bull. New York Acad. Med. 30: 155, 1954. (3) Smith, N. J., and Rosello, S.: J. Clin. Nutrition 1: 275, 1953. (4) Sturgeon, P.: Pediatrics 13: 107, 1954.

MEAD | SYMBOL OF SERVICE IN MEDICINE

MEAD JOHNSON & COMPANY, EVANSVILLE 21, INDIANA, U.S.A.

RAPIDLY EFFECTIVE

BROAD-SPECTRUM ANTIBIOTIC THERAPY

. . . WELL TOLERATED . . .

BY THE INTRAMUSCULAR ROUTE

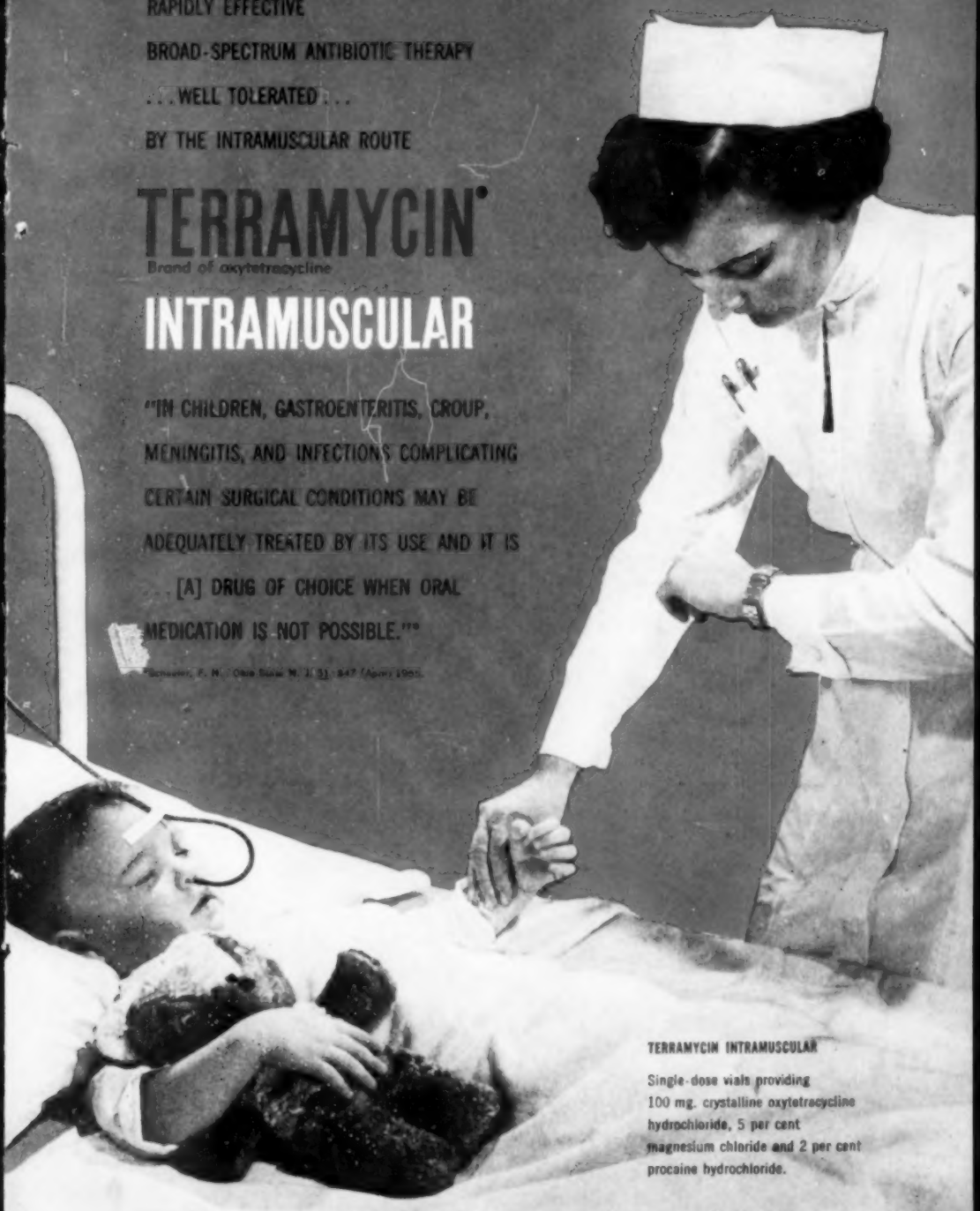
TERRAMYCIN®

Brand of oxytetracycline

INTRAMUSCULAR

"IN CHILDREN, GASTROENTERITIS, CROUP, MENINGITIS, AND INFECTIONS COMPLICATING CERTAIN SURGICAL CONDITIONS MAY BE ADEQUATELY TREATED BY ITS USE AND IT IS . . . [A] DRUG OF CHOICE WHEN ORAL MEDICATION IS NOT POSSIBLE."*

*Schwartz, P. N.: Ohio State M. J. 51: 847 (April) 1955.

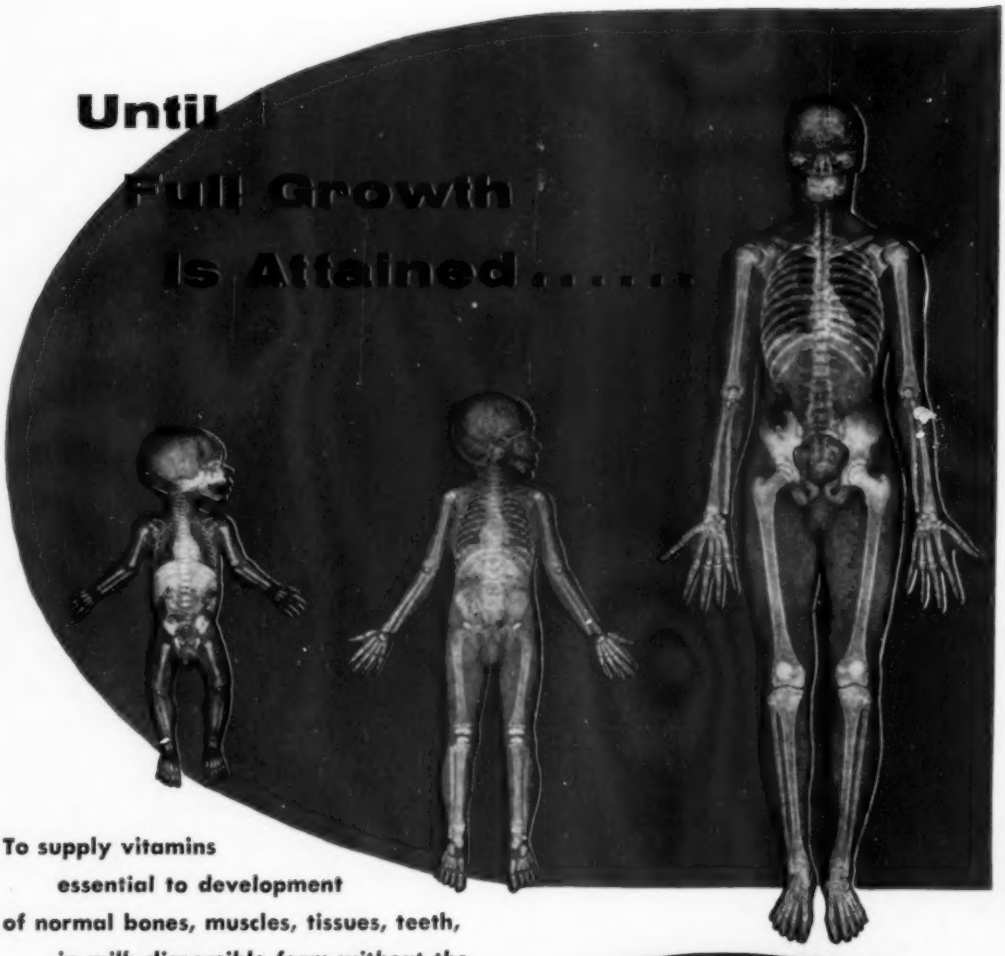


TERRAMYCIN INTRAMUSCULAR

Single-dose vials providing 100 mg. crystalline oxytetracycline hydrochloride, 5 per cent magnesium chloride and 2 per cent procaine hydrochloride.

Pfizer PFIZER LABORATORIES, Division, Chas. Pfizer & Co., Inc., Brooklyn 6, N. Y.

Until Full Growth Is Attained.....



To supply vitamins essential to development of normal bones, muscles, tissues, teeth, *in milk dispersible form without the likelihood of producing allergic reactions:*

Drisdol and Drisdol with A are convenient and pleasant to administer to infants and children. They diffuse completely in milk . . . do not impair its flavor . . . do not separate, float or adhere to bottle or glass . . . may be given in other liquid or solid foods. Since they are *pure synthetic* vitamins, they are not likely to produce allergic reactions.

DRISDOL, bottles of 5, 10 and 50 cc.
DRISDOL with Vitamin A, bottles of 10 and 50 cc.

WINTHROP LABORATORIES
New York 18, N. Y. • Windsor, Ont.

IN PROPYLENE GLYCOL
10,000 units of synthetic vitamin D_2 per Gram
(250 units per drop)
Odorless • Tasteless

DISPERSIBLE
10,000 units of synthetic vitamin D_2, 50,000 units of synthetic vitamin A per gram (250 units vitamin D_2 and 1250 units vitamin A per drop).

Drisdol, trademark reg. U.S. Pat. Off.